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     (FILE 'HOME' ENTERED AT 10:30:21 ON 13 JAN 2000)

     FILE 'HCAPLUS' ENTERED AT 10:30:28 ON 13 JAN 2000
L1          1288 S EPITHELI? (L) CELL# (L) TUMOR#
L2             2 S IMMORTILI?
L3             0 S L1 AND L2
L4          2027 S IMMORTALI?
L5            61 S L1 AND L4
L6         10165 S ONCOGENE#
L7             4 S L5 AND L6
L8          6856 S SV40
L9            15 S L1 AND L8
L10            8 S L9 AND (L6 OR L4)
L11        23762 S RAS OR WT1 OR BCL 2 OR P53MUT OR MYC OR HER 2 NEU OR HPV16
OR
L12           15 S L5 AND L11
L13           27 S L7 OR L9 OR L12
L14         7927 S IMMUNOSTIMU?
L15            1 S L5 AND L14
L16           27 S L15 OR L13
L17        66151 S B7 OR INTERLEUKIN# OR IL (W) (2 OR 4 OR 7) OR IFN  (2W)
(ALPH
L18        66159 S L17 OR CYTOKIN
L19       102602 S L17 OR CYTOKIN?
L20            6 S L5 AND L19
L21           32 S L20 OR L16

=> d .ca 1-32


L21  ANSWER 1 OF 32  HCAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:         1999:438493  HCAPLUS
DOCUMENT NUMBER:          131:193825
TITLE:                    Arsenic trioxide induces apoptosis of HPV16
                          DNA-immortalized human cervical epithelial
                          cells and selectively inhibits viral gene expression
AUTHOR(S):                Zheng, Jie; Deng, You-Ping; Lin, Chen; Fu, Ming;
Xiao,
                          Pei-Gen; Wu, Min
CORPORATE SOURCE:         Department of Cell Biology, Cancer Institute, Chinese
                          Academy of Medical Sciences, Peking Union Medical
                          College, Beijing, Peop. Rep. China
SOURCE:                   Int. J. Cancer (1999), 82(2), 286-292
                          CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER:                Wiley-Liss, Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Arsenic trioxide (As2O3), a major ingredient of arsenic compds. in
     traditional Chinese medicine, exhibits anti-acute promyelocytic leukemic
     activity.  Considering that over 80% of human malignant tumors derive
from
     epithelial cells, we studied the effect of As2O3 on HPV 16
     DNA-immortalized human cervical epithelial cells (HCE16/3 cells) in
vitro.
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As2O3 reduced HCE16/3 cell survival, induced apoptosis at a low concn. and selectively inhibited expression of viral early genes. This effect was evidenced by a redn. of cell viability in the MTT assay, G1 arrest and significant apoptosis upon flow-cytometric anal., presence of apoptotic bodies, formation of DNA ladders upon gel electrophoresis and inhibition of viral early gene expression by RT-PCR and Western blot. There was a good correlation between cell apoptosis and viral early gene inhibition after As2O3 treatment, suggesting that induction of apoptosis of HCE16/3 cells by As2O3 treatment might be assocd. with down-regulation of viral oncogene expression. In conclusion, our findings indicate that As2O3 induces apoptosis of HCE16/3 cells, which may provide a new approach for treating HPV-assocd. tumors.

CC 1-6 (Pharmacology)

ST arsenic trioxide apoptosis **HPV16** cervix epithelium; cervical carcinoma antitumor apoptosis **HPV16 oncogene**

IT **Human papillomavirus 16**
(E7 gene; arsenic trioxide induces apoptosis of **HPV16** DNA-**immortalized** human cervical epithelial cells and selectively inhibits viral gene expression)

IT Apoptosis
Gene expression
(arsenic trioxide induces apoptosis of **HPV16** DNA-**immortalized** human cervical epithelial cells and selectively inhibits viral gene expression)

IT **Oncogenes** (animal)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(arsenic trioxide induces apoptosis of **HPV16** DNA-**immortalized** human cervical epithelial cells and selectively inhibits viral gene expression)

IT Cervical **tumor** inhibitors
(carcinoma; arsenic trioxide induces apoptosis of **HPV16** DNA-**immortalized** human cervical **epithelial cells** and selectively inhibits viral gene expression)

IT Carcinoma inhibitors
(cervical; arsenic trioxide induces apoptosis of **HPV16** DNA-**immortalized** human cervical epithelial cells and selectively inhibits viral gene expression)

IT 1327-53-3, Arsenic trioxide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(arsenic trioxide induces apoptosis of **HPV16** DNA-**immortalized** human cervical epithelial cells and selectively inhibits viral gene expression)

L21 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:387512 HCAPLUS
DOCUMENT NUMBER: 131:165464
TITLE: Growth of HPV-18 **immortalized** human prostatic intraepithelial neoplasia cell lines. Influence of IL-10, follistatin, activin-A, and DHT
AUTHOR(S): Wang, M.; Liu, A.; Garcia, F. U.; Rhim, J. S.; Stearns, M. E.
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, MCP-Hahnemann University, Philadelphia, PA,

19102-1192, USA
SOURCE: Int. J. Oncol. (1999), 14(6), 1185-1195
CODEN: IJONES; ISSN: 1019-6439
PUBLISHER: International Journal of Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cultures from high grade prostatic intraepithelial neoplasia (HGPIN) have been established and immortalized by HPV-18 infection. The cultures were identified as PIN by Western blotting with anti-cytokeratin (34.beta.E12) and prostate specific antigen (PSA) antibodies. We examd. the growth capabilities of the cultures in the presence of TGF-.beta.1, activin-A, follistatin (FS), androgens (DHEA, DHT) and several cytokines (IL-10, IL-2, IL-4). IL-10, FS, and DHT stimulated cell proliferation and colony forming ability, while the other cytokines and growth factors had no discernable effect. In addn., DHT and to a lesser extent IL-10 both stimulated PSA prodn. Activin-A blocked IL-10, FS, and DHT stimulated growth and PSA prodn. We interpret the data to mean that IL-10 induction of FS secretion (and FS binding of activin A) restores the normal growth capabilities of HGPIN cultures.

CC 2-4 (Mammalian Hormones)

ST prostate tumor growth hormone **interleukin**; follistatin prostate tumor growth; activin prostate tumor growth; dihydrotestosterone prostate tumor growth

IT Prostatic **tumors**
(**epithelial** prostatic **tumors**; gonadal hormones and **interleukin**-10 effect on growth of HPV-18 **immortalized** human prostatic intraepithelial neoplasia **cell** lines)

IT **Immortalization**
(gonadal hormones and **interleukin**-10 effect on growth of HPV-18 **immortalized** human prostatic intraepithelial neoplasia cell lines)

IT **Interleukin** 10
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(gonadal hormones and **interleukin**-10 effect on growth of HPV-18 **immortalized** human prostatic intraepithelial neoplasia cell lines)

IT Cell proliferation
(growth factors and **interleukins** effect on growth of HPV-18 **immortalized** human prostatic intraepithelial neoplasia cell lines)

IT **Interleukin** 2
Interleukin 4
Transforming growth factor .beta.1
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(growth factors and **interleukins** effect on growth of HPV-18 **immortalized** human prostatic intraepithelial neoplasia cell lines)

IT Prostate **epithelium**
(**tumors**; gonadal hormones and **interleukin**-10 effect on growth of HPV-18 **immortalized** human prostatic intraepithelial neoplasia **cell** lines)

IT 53-43-0, Dehydroepiandrosterone 521-18-6, Dihydrotestosterone
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(gonadal hormones and **interleukin**-10 effect on growth of

HPV-18 **immortalized** human prostatic intraepithelial neoplasia cell lines)

IT 104625-48-1, Activin-A 117628-82-7, Follistatin
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(growth factors and **interleukins** effect on growth of HPV-18 **immortalized** human prostatic intraepithelial neoplasia cell lines)

L21 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:318891 HCAPLUS
DOCUMENT NUMBER: 131:113183
TITLE: Genomic instability and tumorigenic induction in **immortalized** human bronchial epithelial cells by heavy ions
AUTHOR(S): Hei, T. K.; Piao, C. Q.; Wu, L. J.; Willey, J. C.; Hall, E. J.
CORPORATE SOURCE: Center for Radiological Research, College of Physicians & Surgeons, Columbia University, New York, NY, 10032, USA
SOURCE: Adv. Space Res. (1999), Volume Date 1998, 22(12), 1699-1707
CODEN: ASRSDW; ISSN: 0273-1177
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Carcinogenesis is postulated to be a progressive multistage process characterized by an increase in genomic instability and clonal selection with each mutational event endowing a selective growth advantage. Genomic instability as manifested by the amplification of specific gene fragments is common among tumor and transformed cells. In the present study, immortalized human bronchial (BEP2D) cells were irradiated with graded doses of either 1GeV/nucleon 56Fe ions or 150 keV/.mu.m alpha particles. Transformed cells developed through a series of successive steps before becoming tumorigenic in nude mice. Tumorigenic cells showed neither ras mutations nor deletion in the p16 tumor suppressor gene. In contrast, they harbored mutations in the p53 gene and over-expressed cyclin D1. Genomic instability among transformed cells at various stage of the carcinogenic process was examd. based on frequencies of PALA resistance. Incidence of genomic instability was highest among established tumor cell lines relative to transformed, non-tumorigenic and control cell lines. Treatment of BEP2D cells with a 4 mM dose of the aminothiol WR-1065 significantly reduced their neoplastic transforming response to 56Fe particles. This model provides an opportunity to study the cellular and mol. mechanisms involved in malignant transformation of human epithelial cells by heavy ions.

CC 8-7 (Radiation Biochemistry)
IT Bronchial epithelium
Epithelium
Genotoxicity
Heavy ion beams
Transformation (neoplastic)
(genomic instability and tumorigenic induction in **immortalized** human bronchial epithelial cells by heavy ions)
IT Cyclin D1
p53 gene (animal)

ras gene (animal)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(genomic instability and tumorigenic induction in **immortalized** human bronchial epithelial cells by heavy ions)
IT **Tumor** suppressor genes (animal)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p16; genomic instability and tumorigenic induction in **immortalized** human bronchial **epithelial cells** by heavy ions)
IT 12587-46-1, Alpha particle 14093-02-8D, Iron 56, ion beam, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(genomic instability and tumorigenic induction in **immortalized** human bronchial epithelial cells by heavy ions)
IT 51321-79-0, PALA
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(genomic instability in **immortalized** human bronchial epithelial cells by heavy ions based on frequencies of PALA resistance)

L21 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:814641 HCAPLUS
DOCUMENT NUMBER: 130:221227
TITLE: Nuclear expression of p16CDKN2 gene product in human laryngeal epithelial cells transfected with human papillomavirus type 16 genome
AUTHOR(S): Sugiura, Natsuki; Tsutsumi, Kouichiro; Seki, Yoshitake; Koizuka, Izumi
CORPORATE SOURCE: School of Medicine, St. Marianna University, Sugao, Miyamae-ku, Kawasaki, 216-8511, Japan
SOURCE: Sei Marianna Ika Daigaku Zasshi (1998), 26(4), 435-443
CODEN: SMIZDS; ISSN: 0387-2289
PUBLISHER: Sei-Marianna Ika Daigaku Igakkai
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CDKN2 is a putative tumor suppressor gene and encodes a nuclear protein, p16. The p16 inhibits the D-type cyclin/cyclin dependent kinase complexes that phosphorylate the retinoblastoma protein (pRb), thus blocking G1 cell cycle progression. It has been reported that the expression of p16 is increased in human papillomavirus type 16 (HPV16)-immortalized human epithelial cells. In the present study, the authors examd. the nuclear expression of p16 in cultured human laryngeal epithelial cells (HLECs) by immunocytochem. assay by using a monoclonal antibody against p16. The nuclear expression of p16 was undetectable in untreated normal HLECs. Interestingly, the authors obsd. that the nuclear expression of p16 remained undetectable in pre-immortalized HLECs after transfection with HPV16 genome. Using in situ hybridization assay, the authors confirmed that these pre-immortalized/p16-neg. HLECs clearly expressed HPV16 RNA. Upon immortalization, the nuclear expression of p16 was evident in these HPV16-expressing HLECs. The authors' data suggest that in HLECs, HPV16 expression by itself may be insufficient for the increased expression of p16.
CC 14-1 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 3, 10
ST p16CDKN2 laryngeal epithelium papillomavirus 16 transfection **immortalization**
IT **Tumor** suppressor genes (animal)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CDKN2A; nuclear expression of p16CDKN2 gene product in human laryngeal **epithelial cells** transfected and **immortalized** with human papillomavirus type 16 genome)
IT Epithelium
(disease, infection, larynx; nuclear expression of p16CDKN2 gene product in human laryngeal epithelial cells transfected and **immortalized** with human papillomavirus type 16 genome)
IT Larynx
(epithelium, infection; nuclear expression of p16CDKN2 gene product in human laryngeal epithelial cells transfected and **immortalized** with human papillomavirus type 16 genome)
IT Infection
(epithelium, larynx; nuclear expression of p16CDKN2 gene product in human laryngeal epithelial cells transfected and **immortalized** with human papillomavirus type 16 genome)
IT Respiratory tract infection
(laryngeal epithelial; nuclear expression of p16CDKN2 gene product in human laryngeal epithelial cells transfected and **immortalized** with human papillomavirus type 16 genome)
IT Cell nucleus
Human papillomavirus 16
Immortalization
Transformation (genetic)
Viral infection
(nuclear expression of p16CDKN2 gene product in human laryngeal epithelial cells transfected and **immortalized** with human papillomavirus type 16 genome)
IT p16INK4 protein
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);
BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC
(Process)
(nuclear expression of p16CDKN2 gene product in human laryngeal epithelial cells transfected and **immortalized** with human papillomavirus type 16 genome)
IT Gene expression
Transcription (genetic)
(papillomavirus; nuclear expression of p16CDKN2 gene product in human laryngeal epithelial cells transfected and **immortalized** with human papillomavirus type 16 genome)
IT mRNA
RL: BOC (Biological occurrence); BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
(papillomavirus; nuclear expression of p16CDKN2 gene product in human laryngeal epithelial cells transfected and **immortalized** with human papillomavirus type 16 genome)

L21 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:648556 HCAPLUS

DOCUMENT NUMBER: 130:23477
TITLE: The C terminus of **E1A** regulates **tumor** progression and **epithelial cell** differentiation
AUTHOR(S): Fischer, Robert S.; Quinlan, Margaret P.
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Tennessee, Memphis, TN, 38163, USA
SOURCE: Virology (1998), 249(2), 427-439
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The E1A gene of adenovirus has been considered both a dominant oncogene and a tumor suppressor. It has been reported to induce epithelial cell but to prevent myoblast differentiation. E1A enables oncogenes that are unable to transform primary cells on their own to do so, yet suppresses tumor progression toward invasion and metastasis. To try to reconcile the seemingly, conflicting E1A phenotypes, the authors examd. the expression of epithelial cell specific and characterizing proteins in immortalized or tumorigenically transformed primary epithelial cells expressing wild-type E1A or a C-terminal mutant that has lost tumor suppressive abilities. All the cell types continued to express cytokeratin. Epithelial cell morphol., social behavior, and growth characteristics were retained by cells expressing wild-type E1A, even in the presence of an activated ras oncogene. Mutant E1A-expressing cells were less well differentiated even in the absence of ras. They were specifically defective in cell-cell junctional complexes, such as tight and adherens junctions and desmosomes. There was also a preference for those actin structures prominent in fibroblasts: stress fibers and filopodia, while in the wild-type E1A expressing cells, cortical actin and circumferential actin filaments were dominant. Thus the E1A-mutant-expressing cells were already predisposed to a more advanced tumor stage even when they were only immortalized and not transformed. The results suggest the possibility that the C terminus of E1A may be involved in regulating epithelial mesenchymal transitions, which have previously been linked to tumor progression. (c) 1998 Academic Press.
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3, 10
ST **E1A** gene adenovirus epithelium differentiation transformation; tumor suppression **E1A** gene adenovirus epithelium
IT Adenoviridae
Cell differentiation
Immortalization
Transformation (neoplastic)
(C terminus of adenovirus **E1A** 12S regulates **tumor** progression and **epithelial cell** differentiation)
IT **E1A** gene (microbial)
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(C terminus of adenovirus **E1A** 12S regulates **tumor** progression and **epithelial cell** differentiation)
IT Desmosome
Stress fiber

Tight junction
Viral infection
(C terminus of adenovirus **E1A** 12S regulates **tumor** progression and **epithelial cell** differentiation in relation to)

IT Actins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(C terminus of adenovirus **E1A** 12S regulates **tumor** progression and **epithelial cell** differentiation in relation to)

IT **ras** gene (animal)
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(activated; C terminus of adenovirus **E1A** 12S regulates **tumor** progression and **epithelial cell** differentiation in relation to)

IT **Tumors** (animal)
(**epithelium**; C terminus of adenovirus **E1A** 12S regulates **tumor** progression and **epithelial cell** differentiation)

IT Organelle
(filopodium; C terminus of adenovirus **E1A** 12S regulates **tumor** progression and **epithelial cell** differentiation in relation to)

IT Transcription factors
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(gene **E1a**, 243R (243 amino acid residues); C terminus of adenovirus **E1A** 12S regulates **tumor** progression and **epithelial cell** differentiation)

IT p21ras protein
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p21c-**ras**, activated; C terminus of adenovirus **E1A** 12S regulates **tumor** progression and **epithelial cell** differentiation in relation to)

IT **Epithelium**
(**tumor**; C terminus of adenovirus **E1A** 12S regulates **tumor** progression and **epithelial cell** differentiation)

IT **Cell** junction
(zonula adherens; C terminus of adenovirus **E1A** 12S regulates **tumor** progression and **epithelial cell** differentiation in relation to)

L21 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:598297 HCAPLUS
DOCUMENT NUMBER: 130:2610
TITLE: Nuclear and nucleolar image analysis of human breast epithelial cells transformed by benzo[a]pyrene and transfected with the c-Ha-**ras** **oncogene**
AUTHOR(S): Barbisan, Luis Fernando; Russo, Jose; Mello, Maria Luiza S.
CORPORATE SOURCE: Department of Cell Biology, Institute of Biology, UNICAMP, Campinas, 13083-970, Brazil
SOURCE: Anal. Cell. Pathol. (1998), 16(4), 193-199
CODEN: ACPAER; ISSN: 0921-8912

PUBLISHER: IOS Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Changes in nuclear and nucleolar morphometric parameters were investigated by image anal. procedures in human breast MCF-10F epithelial cells expressing different stages of the tumorigenic progression after benzo[a]pyrene (BP) transformation (BP1, BP1-E, and BP1-E1 cell lines), and addnl. transfected with the c-Ha-ras oncogene (BP1-Tras cell line). Nuclear pleomorphism was evident in all the transformed cells. The anal. of different morphometric parameters did not show a clear relation between specific nuclear and nucleolar changes and the expression of the different stages of the tumorigenesis, with the exception of the nucleolar size, which could be assocd. to the expression of the tumorigenic phenotype, and a nucleolar area/nuclear area ratio, which discriminated the immortalized, the transformed, and the tumorigenic phenotypes from one another. The nuclear morphometric data established for the BP-transformed cells and for the cells addnl. transfected with the c-Ha-ras oncogene were suggestive of complex and distinct morphofunctional mechanisms involving the in vitro transformation of the MCF-10F cells. The nuclear changes found in the BP1-Tras cell line were assumed to be related to the addnl. effects and/or enhanced genomic instability induced by transfection with the ras oncogene.
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3, 4
ST breast epithelial cell transformation benzopyrene cHaras **oncogene** nucleus nucleolus
IT Breast **tumors**
Carcinogens
Cell morphology
Cell nucleolus
Cell nucleus
Immortalization
Mammary epithelium
Phenotypes
Transformation (neoplastic)
(nuclear and nucleolar image anal. of human breast **epithelial cells** transformed by benzo[a]pyrene and transfected with c-Ha-**ras oncogene**)
IT c-Ha-**ras** gene (animal)
p21c-Ha-**ras** protein
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(nuclear and nucleolar image anal. of human breast epithelial cells transformed by benzo[a]pyrene and transfected with c-Ha-**ras oncogene**)
IT 50-32-8, Benzo[a]pyrene, biological studies

RL: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(nuclear and nucleolar image anal. of human breast epithelial cells transformed by benzo[a]pyrene and transfected with c-Ha-**ras** **oncogene**)

L21 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:466425 HCAPLUS
DOCUMENT NUMBER: 129:93575
TITLE: Establishment and characterization of **immortalized** human epithelial cell line from cornea
INVENTOR(S): Offord, Cavin Elizabeth; Tromvoukis, Yvonne; Pfeifer, Andrea M. A.; Sharif, Naj
PATENT ASSIGNEE(S): Societe des Produits Nestle S.A., Switz.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 851028	A1	19980701	EP 1996-203707	19961224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CA 2219038	AA	19980624	CA 1997-2219038	19971113
AU 9748539	A1	19980625	AU 1997-48539	19971222
JP 10215863	A2	19980818	JP 1997-353862	19971222
PRIORITY APPLN. INFO.:			EP 1996-203707	19961224

AB Human corneal epithelial cell lines are established and characterized. The cells are capable of expressing .gtoreq.2 metabolic markers such as vimentin, cytokeratins, cytochrome P 450, glutathione-S-transferase, Cu/Zn superoxide dismutase, glutathione peroxidase, aldehyde reductase, and catalase. Other markers include cytokines and growth factors. The established corneal cell lines, including CNCM 1-1777, can be used to study or assay toxicity or mutagenicity of pharmaceutical compds.
IC ICM C12N005-10
ICS G01N033-50; C12Q001-68; A61K035-44
CC 13-7 (Mammalian Biochemistry)
Section cross-reference(s): 63
ST corneal epithelial cell human **immortalization**; **cytokine** growth factor epithelial cell line
IT Animal cell line
(CNCM1-1777; establishment and characterization of **immortalized** human epithelial cell line from cornea)
IT Cornea (eye)
Epithelium
Immortalization
(establishment and characterization of **immortalized** human epithelial cell line from cornea)
IT **Interleukin** 1 receptor antagonist
Interleukin 1.alpha.
Interleukin 1.beta.
Interleukin 6

Interleukin 8
Keratins
Transforming growth factor .beta.1
Transforming growth factor .beta.2
Tumor necrosis factor .alpha.
Vimentins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(establishment and characterization of **immortalized** human **epithelial cell** line from cornea)

IT Platelet-derived growth factors
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(.beta.; establishment and characterization of **immortalized** human epithelial cell line from cornea)

IT 9001-05-2, Catalase 9001-48-3, Glutathione reductase 9013-66-5, Glutathione peroxidase 9028-12-0, Aldehyde reductase 9054-89-1, Superoxide dismutase
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(Copper-zinc; establishment and characterization of **immortalized** human epithelial cell line from cornea)

IT 9035-51-2, Cytochrome p450, biological studies 50812-37-8, Glutathione S-transferase 62229-50-9, Epidermal growth factor
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(establishment and characterization of **immortalized** human epithelial cell line from cornea)

IT 83869-56-1, Gm-csf
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(.beta.; establishment and characterization of **immortalized** human epithelial cell line from cornea)

L21 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:453588 HCAPLUS
DOCUMENT NUMBER: 129:211824
TITLE: Sex hormones are weak regulators of **HPV16** DNA-**immortalized** human uterine exocervical epithelial cells
AUTHOR(S): Zheng, Jie
CORPORATE SOURCE: Department of Pathology, Nanjing Railway Medical College, Nanjing, 210009, Peop. Rep. China
SOURCE: Chin. Med. J. (Beijing, Engl. Ed.) (1998), 111(4), 364-367
CODEN: CMJODS; ISSN: 0366-6999
PUBLISHER: Chinese Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objective of this study was to examine the effect of sex hormones on the growth and gene expression of human papilloma virus (HPV) type 16 DNA-immortalized human uterine cervical epithelial cells (HCE16/3 cells). The effect of sex hormones on the growth and viral gene expression of HCE16/3 cells was studied using [3H]-thymidine incorporation, soft agarose assay and Northern blot anal. The growth of HCE16/3 cells was found to be

little affected by estradiol and progesterone while insulin was a mitogen for HCE16/3 cells in phenol red-free medium with steroid-stripped serum. Furthermore, synergistic effects between insulin and hormones were not obsd. Estradiol could not induce the growth of HCE16/3 cell line in soft agarose, either. In Northern blot anal., however, the hormones upregulated the HPV 16 early gene expression in HCE16/3 cells, which was generally considered to be required for the proliferation of HPV DNA-immortalized cells. These results suggest that the proliferation of HCE16/3 cells is still dependent on growth factors and sex hormones upregulate the HPV 16 early gene expression.

CC 2-4 (Mammalian Hormones)

IT Cell proliferation
(sex hormones an insulin effect on proliferation of **HPV16** DNA-**immortalized** human uterine exocervical epithelial cells)

IT Cervical **tumors**
DNA formation
Gene expression
Human papillomavirus 16
(sex hormones are weak regulators of **HPV16** DNA-**immortalized** human uterine exocervical **epithelial cells**)

IT 9004-10-8, Insulin, biological studies
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(sex hormones an insulin effect on proliferation of **HPV16** DNA-**immortalized** human uterine exocervical epithelial cells)

IT 50-28-2, Estradiol, biological studies 57-83-0, Progesterone, biological studies
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(sex hormones are weak regulators of **HPV16** DNA-**immortalized** human uterine exocervical epithelial cells)

L21 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:358145 HCAPLUS
DOCUMENT NUMBER: 129:14147
TITLE: Production of inflammatory mediators and cytokine responsiveness of an **SV40**-transformed human proximal tubular epithelial cell line
AUTHOR(S): Gerritsma, Jort S. J.; Van Kooten, Cees; Gerritsen, Arnout F.; Mommaas, A. Mieke; Van Es, Leendert A.; Daha, Mohamed R.
CORPORATE SOURCE: Department Nephology, Leiden University, Leiden, 2300 RC, Neth.
SOURCE: Exp. Nephrol. (1998), 6(3), 208-216
CODEN: EXNEEG; ISSN: 1018-7782
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Proximal tubular epithelial cells (PTEC) play a central role in the physiol. of the renal tubulointerstitium. To study the relationship between tubular cells and inflammatory renal diseases the availability of cultured cells is of importance. This study describes an immortalized proximal tubular epithelial cell line which was generated using SV40 DNA. To det. whether the transformation altered the cell line, the transformed cell line was characterized phenotypically using different monoclonal

antibodies directed against peptidases, which are characteristic of FTEC, such as adenosine deaminase binding protein (CD26), Leu amino peptidase and carboxy peptidase M by immunofluorescent staining and FACS anal. All peptidases were clearly present on the parental cell line and the transformed cell line. The level of expression of the peptidases was lower on the transformed cell line as compared to the parental nontransfected cells. The morphol. of the transformed cell line, detd. using a transwell culture system and electron microscopy, showed a polarized morphol. of the tubular cells, tight junctions and microvilli. The transformed cell line was compared with the parental proximal tubular epithelial cells in its ability to respond to inflammatory cytokines such as IL-1.alpha., TNF-.alpha., IFN-.gamma.. Stimulation with these cytokines resulted in enhanced prodn. of complement components C2, C3, C4,
and factor H, IL-6 and the chemokines IL-8 and MCP-1. The transformed cell line responded in a similar fashion as the parental cell line, although the amt. of the different proteins produced was higher in the transformed cell line. The transformed tubular cell line seems to be a suitable model to study different effects on tubular cells in relation to inflammatory kidney diseases.

CC 9-11 (Biochemical Methods)

IT Animal cell line
(PTEC-L, PTEC-TRL; inflammatory mediators and cytokine responsiveness of an **SV40**-transformed human proximal tubular epithelial cell line)

IT Cytokines
Interferon .gamma.
Interleukin 1.alpha.
Tumor necrosis factor .alpha.
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(inflammatory mediators and cytokine responsiveness of an **SV40**-transformed human proximal tubular **epithelial cell** line)

IT Interleukin 6
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(inflammatory mediators and cytokine responsiveness of an **SV40**-transformed human proximal tubular epithelial cell line)

IT Interleukin 8
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(inflammatory mediators and cytokine responsiveness of an **SV40**-transformed human proximal tubular epithelial cell line)

IT Monocyte chemoattractant protein-1
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(inflammatory mediators and cytokine responsiveness of an **SV40**-transformed human proximal tubular epithelial cell line)

IT CD40 (antigen)
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(proteins of a **SV40**-transformed human proximal tubular epithelial cell line PTEC-L and PTEC-TRL)

IT 9031-96-3, Peptidase
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)

(Membrane-bound; proteins of a **SV40**-transformed human proximal tubular epithelial cell line PTEC-L and PTEC-TRL)

IT 80295-40-5, Complement C2 80295-41-6, Complement C3 80295-48-3, Complement C4 80295-65-4, Complement factor H
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(inflammatory mediators and cytokine responsiveness of an **SV40**-transformed human proximal tubular epithelial cell line)

IT 9001-61-0, Leucine amino peptidase 120038-28-0, Carboxy peptidase M
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(proteins of a **SV40**-transformed human proximal tubular epithelial cell line PTEC-L and PTEC-TRL)

L21 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:325947 HCAPLUS
DOCUMENT NUMBER: 129:52862
TITLE: Molecular cytogenetic alterations in the early stage at human bronchial epithelial cell carcinogenesis
AUTHOR(S): Dong, Xiang-Yang; Lu, Yong-Jie; Tong, Tong; Wang, Yong-Jun; Guo, Su-Ping; Bai, Jin-Feng; Han, Nai-Jun; Cheng, Shu-Jun
CORPORATE SOURCE: Department of Etiology and Chemical Carcinogenesis, Cancer Institute (Hospital), CAMS & PUMC, Beijing, Peop. Rep. China
SOURCE: J. Cell. Biochem. (1998), Volume Date 1997, (Suppl. 28/29), 74-80
CODEN: JCEBD5; ISSN: 0730-2312
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lung carcinogenesis is a multi-step process involving activation of oncogenes and inactivation of tumor suppressor genes. Many mol. and cytogenetic alterations occur in the early stages of carcinogenesis. We have developed an effective culture system for human bronchial epithelial cells and lung cancer cells. Four immortalized human bronchial epithelial cell lines were established by transfecting the epithelial cells with plasmid DNA contg. the early region of SV40. Some mol. and cytogenetic alterations, such as 3p-, 2q-, 9p-, c-myc translocation t(8;14) (q23; q32), were found in one immortalized bronchial epithelial cell line M when approaching malignant transformation. An increase in cell proliferation and decrease of apoptosis were noted in the late passages of the immortalized cell line M. Some mol. cytogenetic alterations were also obsd. in human primary non-small cell lung cancers. Mol. cytogenetic alterations during the early stage of carcinogenesis of human bronchial epithelial cells may be useful as biomarkers for both diagnosis and intermediate endpoint of chemoprevention of lung cancer.

CC 14-1 (Mammalian Pathological Biochemistry)

IT Apoptosis
Bronchial epithelium
Chromosomal translocation
Cytogenetics
Deletion (mutation)
Immortalization
Lung **tumors**

Non-small-cell carcinoma (lung)
Transformation (neoplastic)
(mol. cytogenetic alterations in early stage at human bronchial **epithelial cell** carcinogenesis)
IT c-**myc** gene (animal)
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(mol. cytogenetic alterations in early stage at human bronchial epithelial cell carcinogenesis)

L21 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:188417 HCAPLUS
DOCUMENT NUMBER: 128:280530
TITLE: Metastatic sublines of an **SV40** large T antigen immortalized human prostate epithelial cell line
AUTHOR(S): Bae, Victoria L.; Jackson-Cook, Colleen K.; Maygarden, Susan J.; Plymate, Steven R.; Chen, Juza; Ware, Joy L.
CORPORATE SOURCE: Department of Pathology, Medical College of Virginia Campus, Richmond, VA, 23298, USA
SOURCE: Prostate (N. Y.) (1998), 34(4), 275-282
CODEN: PRSTDS; ISSN: 0270-4137
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The available human prostate cancer cell lines that are metastatic in athymic nude mice all have complex, highly aneuploid karyotypes. Other prostatic cells immortalized by transforming genes of SV40 or HPV and converted to tumorigenicity by addnl. genetic manipulation are not reported to be metastatic. Tumorigenic sublines of human prostate epithelial cells previously immortalized by transfection with the SV40 T antigen gene were obtained by sequential passage in male athymic nude mice. These sublines were evaluated histopathol. for tumorigenicity and metastasis in athymic nude mice after s.c., i.p., and intraprostatic injection. Each subline was characterized by std. (GTG-banding) cytogenetic and FISH anal., and RNase protection assays for androgen receptor expression. Two sublines produced metastases in lungs and the diaphragm of most mice after either intraprostatic or i.p. injection. The M2205 subline formed large local tumors after intraprostatic injection. Cytogenetic aberrations present in the metastatic sublines, but not in the tumorigenic, nonmetastatic lines or the parental P69SV40T line, included dup(11)(q14q22),der(16)t(16;19)(q24;q13.1), which resulted in the loss of the short arm and proximal long arm of chromosome 19 (19q13.1.fwdarw.19pter), and loss of the Y chromosome. None of the sublines expressed the androgen receptor. These cytogenetically defined, SV40 T-immortalized human prostate epithelial cell lines, with distinct biol. behaviors in vivo, provide addnl. tools for the genetic anal. of the emergence of metastatic capacity.
CC 9-11 (Biochemical Methods)
Section cross-reference(s): 14
ST metastatic subline prostate epithelium **SV40** immortalization; T antigen prostate epithelium immortalization metastasis
IT Animal cell line

(M12; metastatic sublines of **SV40** large T antigen immortalized human prostate epithelial cell line)
IT Animal cell line
(M15; metastatic sublines of **SV40** large T antigen immortalized human prostate epithelial cell line)
IT Animal cell line
(M2205; metastatic sublines of **SV40** large T antigen immortalized human prostate epithelial cell line)
IT Prostatic carcinoma
(metastasis; metastatic sublines of **SV40** large T antigen immortalized human prostate epithelial cell line)
IT Immortalization
Simian virus 40
(metastatic sublines of **SV40** large T antigen immortalized human prostate epithelial cell line)
IT Androgen receptors
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(metastatic sublines of **SV40** large T antigen immortalized human prostate epithelial cell line)
IT Large T antigen
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(metastatic sublines of **SV40** large T antigen immortalized human prostate epithelial cell line)
IT Metastasis (**tumor**)
(prostatic carcinoma; metastatic sublines of **SV40** large T antigen immortalized human prostate **epithelial cell** line)

L21 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:773720 HCAPLUS
DOCUMENT NUMBER: 128:73631
TITLE: Type-1 insulin-like growth factor receptor reexpression in the malignant phenotype of **SV40**-T-immortalized human prostate epithelial cells enhances apoptosis
AUTHOR(S): Plymate, Stephen R.; Bae, Victoria L.; Maddison, Lisette; Quinn, LeBris S.; Ware, Joy L.
CORPORATE SOURCE: Geriatric Res. Education, Clinical Center, American Lake/Seattle VAMC, Tacoma, WA, USA
SOURCE: Endocrine (1997), 7(1), 119-124
CODEN: EOCRE5; ISSN: 1355-008X
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The author have previously shown that the type 1 insulin-like growth factor receptor (IGF-1R) is decreased in the transformation from benign to malignant human prostate epithelial cells in vivo. Further, in a well described human SV40-T immortalized human epithelial cell system beginning with the immortalized, but rarely tumorigenic P69SV40-T cell line, to the highly tumorigenic and metastatic M12 subline, there is a similar decrease in IGF-1R no. from 2.0.times.104 receptors per cell to 1.1.times.103 receptors per cell. When the IGF-1R was reexpressed in the M12 subline

using a retroviral expression vector, M12-LISN, to a receptor no. similar to that of the P69SV40-T parental cell line, the authors demonstrated a marked decrease in colony formation in soft agar in the M12-LISN cell vs. the M12 control cells, and a decrease in vivo tumor growth and metastases when injected either s.c. or an intraprostatic location. This decrease in tumor vol. was not because of a decrease in proliferative capacity, but was assocd. with an increase in apoptosis in baseline cultures and in response to the apoptotic-inducing agents 6-hydroxyurea, retinoic acid, and transforming growth factor .beta.1.

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2

IT Apoptosis
Prostate epithelium
Prostatic **tumors**
Transformation (neoplastic)
(type-1 insulin-like growth factor receptor reexpression in malignant phenotype of **SV40**-T-immortalized human prostate **epithelial cells** enhances apoptosis)

IT Insulin-like growth factor I receptors
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(type-1 insulin-like growth factor receptor reexpression in malignant phenotype of **SV40**-T-immortalized human prostate epithelial cells enhances apoptosis)

IT 67763-96-6, Insulin-like growth factor I
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(receptors; type-1 insulin-like growth factor receptor reexpression in malignant phenotype of **SV40**-T-immortalized human prostate epithelial cells enhances apoptosis)

L21 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:560265 HCAPLUS
DOCUMENT NUMBER: 127:246315
TITLE: Characterization of prostatic epithelial cell lines derived from transgenic adenocarcinoma of the mouse prostate (TRAMP) model
AUTHOR(S): Foster, Barbara A.; Gingrich, Jeffrey R.; Kwon, Eugene D.; Madias, Christopher; Greenberg, Norman M.
CORPORATE SOURCE: Department of Cell Biology, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Cancer Res. (1997), 57(16), 3325-3330
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To develop a syngeneic transplantable system to study immunotherapeutic approaches for the treatment of prostate cancer, three cell lines were established from a heterogeneous 32 wk tumor of the transgenic adenocarcinoma mouse prostate (TRAMP) model. TRAMP is a transgenic line of C57BL/6 mice harboring a construct comprised of the minimal -426/+28 rat probasin promoter driving prostate-specific epithelial expression of the SV40 large T antigen. TRAMP males develop histol. prostatic intraepithelial neoplasia by 8-12 wk of age that progress to adenocarcinoma with distant metastases by 24-30 wk of age. The three cell

lines (TRAMP-C1, TRAMP-C2, and TRAMP-C3) express cytokeratin, E-cadherin, and androgen receptor by immunohistochem. anal. and do not appear to have a mutated p53. Although TRAMP-C1 and TRAMP-C2 are tumorigenic when grafted into syngeneic C57BL/6 hosts, TRAMP-C3 grows readily in vitro but does not form tumors. The T antigen oncoprotein is not expressed by the cell lines in vitro or in vivo. The rationale for establishing multiple cell lines was to isolate cells representing various stages of cellular transformation and progression to androgen-independent metastatic disease that could be manipulated in vitro and, in combination with the TRAMP model, provide a system to investigate therapeutic interventions, such as immunotherapy prior to clin. trials.

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1, 9, 15

IT Prostatic carcinoma inhibitors
(adenocarcinoma; characterization of prostatic epithelial cell lines derived from **SV40** large T antigen transgenic adenocarcinoma of mouse prostate (TRAMP) model in relation to)

IT Disease models
Gene expression
Immunotherapy
Prostatic adenocarcinoma
Simian virus 40
Transcription (genetic)
Transformation (neoplastic)
(characterization of prostatic epithelial cell lines derived from **SV40** large T antigen transgenic adenocarcinoma of mouse prostate (TRAMP) model)

IT Genes (microbial)
Transgenes
mRNA
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);
BUU (Biological use, unclassified); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(characterization of prostatic epithelial cell lines derived from **SV40** large T antigen transgenic adenocarcinoma of mouse prostate (TRAMP) model)

IT Large T antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(characterization of prostatic epithelial cell lines derived from **SV40** large T antigen transgenic adenocarcinoma of mouse prostate (TRAMP) model)

IT Androgen receptors
E-cadherin
Keratins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(expression of; characterization of prostatic epithelial cell lines derived from **SV40** large T antigen transgenic adenocarcinoma of mouse prostate (TRAMP) model)

IT Metastasis (**tumor**)
(from prostatic adenocarcinoma; characterization of prostatic **epithelial cell** lines derived from **SV40** large T antigen transgenic adenocarcinoma of mouse prostate (TRAMP) model)

IT Prostatic adenocarcinoma
(metastasis; characterization of prostatic epithelial cell lines

derived from **SV40** large T antigen transgenic adenocarcinoma of mouse prostate (TRAMP) model)

IT p53 (protein)
p53 gene (animal)
RL: BOC (Biological occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(mutation; characterization of prostatic epithelial cell lines derived from **SV40** large T antigen transgenic adenocarcinoma of mouse prostate (TRAMP) model)

IT Mutation
(p53; characterization of prostatic epithelial cell lines derived from **SV40** large T antigen transgenic adenocarcinoma of mouse prostate (TRAMP) model)

IT Metastasis (**tumor**)
(prostate gland adenocarcinoma; characterization of prostatic **epithelial cell** lines derived from **SV40** large T antigen transgenic adenocarcinoma of mouse prostate (TRAMP) model)

IT Adenocarcinoma inhibitors
(prostatic; characterization of prostatic epithelial cell lines derived from **SV40** large T antigen transgenic adenocarcinoma of mouse prostate (TRAMP) model in relation to)

L21 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:530864 HCAPLUS
DOCUMENT NUMBER: 127:232675
TITLE: Two distinct human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA
AUTHOR(S): Ohta, Yujiro; Tsutsumi, Kouichiro; Kikuchi, Keiji; Yasumoto, Shigeru
CORPORATE SOURCE: Department of Gynecology, Nippon Medical School, Tokyo, 113, Japan
SOURCE: Jpn. J. Cancer Res. (1997), 88(7), 644-651
CODEN: JJCREP; ISSN: 0910-5050
PUBLISHER: Japanese Cancer Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have established two distinct human cervical cell lines, NCC16 and NCE16, after transfecting human papillomavirus type 16 (HPV16) DNA into normal human ecto-cervical and endo-cervical epithelial cells, resp. Both lines expressed HPV16 E6 and E7 as detected by reverse transcriptase-polymerase chain reaction and northern blot hybridization. These cells have been passaged for over 100 population doublings and express strong telomerase activity. Neither cell line was tumorigenic in athymic nu/nu mice. However, both NCC16 and NCE16 developed abnormally stratified architectures following implantation with a silicon membrane sheet in the back of athymic nude mice. The former cells were pathohistol. similar to carcinoma, while the latter produced Alcian-blue pos. cells, suggesting the occurrence of metaplastic changes. These distinct cell lines offer a useful model system for the study of cervical carcinogenesis and of its regulatory mechanism after HPV infection in different regions of the uterine cervix.

CC 14-1 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 3, 9, 10
IT Animal cell line
(NCC16; human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)
IT Animal cell line
(NCE16; human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)
IT Keratinocyte
(disease, infection, ecto-cervical; human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)
IT Keratinocyte
(ecto-cervical; human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)
IT Cervix (uterus)
(ectocervical epithelium; human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)
IT Uterine epithelium
(ectocervical; human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)
IT Cell infection (animal)
Cervical **tumors**
Disease models
Endometrial epithelium (uterus)
Gene expression
Human papillomavirus 16
Immortalization
Transcription (genetic)
Transformation (genetic)
Viral infection
(human uterine cervical **epithelial cell** lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)
IT mRNA
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)
IT E6 gene (microbial)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16**

DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)

IT E7 gene (microbial)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)

IT Viral DNA
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)

IT Skin infection
(keratinocyte, ecto-cervical; human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)

IT E6 protein
E7 protein
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mRNA for; human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)

IT 120178-12-3, Nucleotidyltransferase, terminal deoxyribo-(telomeric DNA)
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(human uterine cervical epithelial cell lines established after transfection with **human papillomavirus 16** DNA for model of cervical carcinogenesis in relation to E6, E7, and telomerase expression)

L21 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:474431 HCAPLUS
DOCUMENT NUMBER: 127:158704
TITLE: Characterization of human amniotic epithelial cells transformed with origin-defective **SV40** T-antigen gene
AUTHOR(S): Tohyama, Jun; Tsunoda, Hiroyuki; Sakuragawa, Norio
CORPORATE SOURCE: Department of Inherited Metabolic Disease, National Center of Neurology and Psychiatry, National Institute of Neuroscience, Kodaira, 187, Japan
SOURCE: Tohoku J. Exp. Med. (1997), 182(1), 75-82
CODEN: TJEMAO; ISSN: 0040-8727
PUBLISHER: Tohoku University Medical Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This paper describes characteristics of human amniotic epithelial cells (AEC) transfected with a gene of origin-defective simian virus (SV) 40 large T-antigen (pMTIOD). Normal AEC before transfection with pMTIOD exhibited only low proliferative potential under the authors' culture conditions. AEC cells transfected with pMTIOD exhibited greater proliferative potentials. Flow cytometry and immunohistochem. analyses

showed that both the primary and the transfected AEC did not express appreciable levels of class II antigens. However, the expression of class I antigen of the transfected AEC cells was slightly increased. The cells obtained in this expt. have the ability to induce tumors in severely combined immunodeficiency mice. Apparently, established AEC line can be used as a tool to investigate possible expression of the desired gene in human AEC and the gene products, however, was not suitable as a gene carrier to the recipient. Further expts. will be required to establish AEC as a transgene carrier for somatic cell gene therapy.

CC 9-11 (Biochemical Methods)
Section cross-reference(s): 1, 3, 10

ST amniotic epithelium transformation **SV40** T gene

IT Mouse
(SCID; characterization of human amniotic epithelial cells transformed with origin-defective **SV40** T-antigen gene)

IT Epithelium
(amniotic epithelium; immunol. characterization of human amniotic epithelial cells transformed with origin-defective **SV40** T-antigen gene)

IT Cell proliferation
Enzyme replacement therapy
Fetus
Gene therapy
Simian virus 40
Transformation (genetic)
Transformation (neoplastic)
Tumors (animal)
(characterization of human amniotic **epithelial cells** transformed with origin-defective **SV40** T-antigen gene)

IT Class II HLA antigens
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(characterization of human amniotic epithelial cells transformed with origin-defective **SV40** T-antigen gene)

IT Amnion
(epithelium; immunol. characterization of human amniotic epithelial cells transformed with origin-defective **SV40** T-antigen gene)

IT Large T antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene; characterization of human amniotic epithelial cells transformed with origin-defective **SV40** T-antigen gene)

IT Class I HLA antigens
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(immunol. characterization of human amniotic epithelial cells transformed with origin-defective **SV40** T-antigen gene)

IT Metabolic diseases
(inborn; characterization of human amniotic epithelial cells transformed with origin-defective **SV40** T-antigen gene)

IT Genes (microbial)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(large T antigen; characterization of human amniotic epithelial cells transformed with origin-defective **SV40** T-antigen gene)

L21 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:419674 HCAPLUS
DOCUMENT NUMBER: 127:134021
TITLE: Androgen responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18
AUTHOR(S): Bello, Diana; Webber, Mukta M.; Kleinman, Hynda K.; Wartinger, David D.; Rhim, Johng S.
CORPORATE SOURCE: Departments of Medicine and Zoology, Michigan State University, East Lansing, MI, 48824-1312, USA
SOURCE: Carcinogenesis (1997), 18(6), 1215-1223
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Prostate cancer and benign tumors of the prostate are the two most common neoplastic diseases in men in the United States, however, research on their causes and treatment has been slow because of the difficulty in obtaining fresh samples of human tissue and a lack of well characterized cell lines which exhibit growth and differentiation characteristics of normal prostatic epithelium. Non-neoplastic adult human prostatic epithelial cells from a white male donor were immortalized with human papillomavirus 18 which resulted in the establishment of the RWPE-1 cell line. Cells from the RWPE-1 cell line were further transformed by v-Ki-ras to establish the RWPE-2 cell line. The objectives of this study were to: (1) establish the prostatic epithelial origin and androgen responsiveness of RWPE-1 and RWPE-2 cell lines; (2) examine their response to growth factors; and (3) establish the malignant characteristics of the RWPE-2 cell line. Immunoperoxidase staining showed that both RWPE-1 and RWPE-2 cells express cytokeratins 8 and 18, which are characteristic of luminal prostatic epithelial cells, but they also coexpress basal cell cytokeratins. These cell lines show growth stimulation and prostate specific antigen (PSA) and androgen receptor (AR) expression in response to the synthetic androgen mibolerone, which establishes their prostatic epithelial origin. Both cell lines also show a dose-dependent growth stimulation by EGF and bFGF and growth inhibition when exposed to TGF-.beta., however, the transformed RWPE-2 cells are less responsive. RWPE-1 cells neither grow in agar nor form tumors when injected into nude mice with or without Matrigel. However, RWPE-2 cells form colonies in agar and tumors in nude mice. In the in vitro invasion assay, RWPE-1 cells are not invasive whereas RWPE-2 cells are invasive. Nuclear expression of p53 and Rb proteins was heterogeneous but detectable by immunostaining in both cell lines. The RWPE-1 cells, which show many normal cell characteristics, and the malignant RWPE-2 cells, provide useful cell culture models for studies on prostate growth regulation and carcinogenesis.
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2, 3, 9
IT Keratins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(14; protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)
IT Keratins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU

(Occurrence)
(18; protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

IT Keratins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(8; protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

IT Animal cell line
(RWPE-1; protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

IT Animal cell line
(RWPE-2; protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human.papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

IT Cell migration
(invasion; protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

IT Keratins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(keratin 5; protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

IT Basement membrane
Cell proliferation
Disease models
Human papillomavirus 18
Immortalization
Prostate epithelium
Prostatic **tumors**
Transformation (neoplastic)
(protein expression and growth factor responsiveness of androgen-responsive adult human prostatic **epithelial cell** lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

IT Androgens
Rb protein
Transforming growth factors .beta.
p53 (protein)
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

IT Androgen receptors

RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

IT Prostate-specific antigen
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

IT Genes (microbial)
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);
BUU (Biological use, unclassified); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(v-Ki-**ras**; protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

IT 62229-50-9, Epidermal growth factor 106096-93-9, Basic fibroblast growth factor
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(protein expression and growth factor responsiveness of androgen-responsive adult human prostatic epithelial cell lines **immortalized** by human papillomavirus 18 and transformed by v-Ki-**ras** in relation to carcinogenesis)

L21 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:172481 HCAPLUS
DOCUMENT NUMBER: 126:167459
TITLE: **Immortalization** of **epithelial tumor cell** with metastatic potential by introducing **oncogene** and use for developing diagnostics
INVENTOR(S): Dickmanns, Achim; Fanning, Ellen; Pantel, Klaus; Riethmueller, Gerhard
PATENT ASSIGNEE(S): Micromet Gmbh, Germany; Dickmanns, Achim; Fanning, Ellen; Pantel, Klaus; Riethmueller, Gerhard
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9700946	A1	19970109	WO 1996-EP2747	19960624

W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2224797	AA	19970109	CA 1996-2224797	19960624	
AU 9664153	A1	19970122	AU 1996-64153	19960624	
EP 839183	A1	19980506	EP 1996-923904	19960624	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 11507834	T2	19990713	JP 1996-503590	19960624	
NO 9706036	A	19980203	NO 1997-6036	19971222	
PRIORITY APPLN. INFO.:			EP 1995-109860	19950623	
			WO 1996-EP2747	19960624	

AB A method for immortalizing epithelial tumor cells with metastatic potential is described by integrating and expressing in the tumor cells an immortalizing oncogene and, optionally, a gene encoding an immuno-stimulatory factor. The invention further relates to antibodies which specifically recognize the epithelial tumor cells of the invention, to processes for the prodn. of said tumor cells as well as pharmaceutical and diagnostic compns. comprising said tumor cells and antibodies, resp. Finally the present invention relates to the use of the epithelial tumor cells and/or antibodies of the invention for the prepn. of tumor vaccines and medicaments for the prophylaxis and/or treatment of cancer and/or the metastasis of cancer. Immortalization of epithelial tumor cells from patients with prostate cancer, renal cell caner, etc., using SV40 large T antigen was shown.

IC ICM C12N005-10
ICS C07K016-30; A61K039-00; A61K039-395; G01N033-53
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 14

ST **immortalization** human **epithelium tumor cell oncogene**

IT **Immunostimulants**
(co-transformation of **epithelial tumor cells** with **oncogene** and; **immortalization** of **epithelial tumor cell** with metastatic potential by introducing **oncogene** and use for developing diagnostics)

IT Antitumor agents
(development of; **immortalization** of **epithelial tumor cell** with metastatic potential by introducing **oncogene** for developing diagnostics)

IT Bone marrow
(**epithelial tumor cells** derived from; **immortalization** of **epithelial tumor cell** with metastatic potential by introducing **oncogene** and use for developing diagnostics)

IT Genetic elements
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene **E1A** RNA formation factor-responsive element, **immortalizing** agent; **immortalization** of **epithelial tumor cell** with metastatic potential by introducing **oncogene** for developing diagnostics)

IT Diagnosis
Epithelium

Immortalization
Metastasis (**tumor**)
(**immortalization** of **epithelial tumor**
cell with metastatic potential by introducing **oncogene**
and use for developing diagnostics)
IT **WT1** gene (animal)
bcl-2 gene (animal)
ras gene (animal)
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); BIOL (Biological study); USES (Uses)
(**immortalizing** agent; **immortalization** of
epithelial tumor cell with metastatic
potential by introducing **oncogene** and use for developing
diagnostics)
IT Human papillomavirus 18
(**immortalizing** agent; **immortalization** of
epithelial tumor cell with metastatic
potential by introducing **oncogene** for developing diagnostics)
IT c-erbB2 gene (animal)
c-**myc** gene (animal)
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); BIOL (Biological study); USES (Uses)
(**immortalizing** agent; **immortalization** of
epithelial tumor cell with metastatic
potential by introducing **oncogene** for developing diagnostics)
IT Large T antigen
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); BIOL (Biological study); USES (Uses)
(of **SV40**; **immortalizing** agent;
immortalization of **epithelial tumor**
cell with metastatic potential by introducing **oncogene**
and use for developing diagnostics)
IT Genes (animal)
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); BIOL (Biological study); USES (Uses)
(**p53mut**; **immortalizing** agent;
immortalization of **epithelial tumor**
cell with metastatic potential by introducing **oncogene**
for developing diagnostics)
IT Monoclonal antibodies
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(to human **epithelial tumor cells**;
immortalization of **epithelial tumor**
cell with metastatic potential by introducing **oncogene**
for developing diagnostics)
IT Genes
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); BIOL (Biological study); USES (Uses)
(transforming; **immortalization** of **epithelial**
tumor cell with metastatic potential by introducing
oncogene and use for developing diagnostics)

IT Vaccines
(**tumor; immortalization** of **epithelial tumor cell** with metastatic potential by introducing **oncogene** for developing diagnostics)
IT Human papillomavirus
(type 16; **immortalizing** agent of; **immortalization** of **epithelial tumor cell** with metastatic potential by introducing **oncogene** for developing diagnostics)

L21 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:168784 HCAPLUS
DOCUMENT NUMBER: 126:262459
TITLE: Expression of estrogen receptors in a normal human breast epithelial cell type with luminal and stem cell characteristics and its neoplastically transformed cell lines
AUTHOR(S): Kang, Kyung-Sun; Morita, Ikue; Cruz, Angela; Jeon, Young Jin; Trosko, James E.; Chang, Chia-Cheng
CORPORATE SOURCE: Department Pediatrics/Human Development, Michigan State University, East Lansing, MI, 48824-1317, USA
SOURCE: Carcinogenesis (1997), 18(2), 251-257
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although approx. two-thirds of breast cancers are estrogen receptor (ER)-pos., only a small proportion of epithelial cells in the mammary gland express the ER. The origin of the ER-pos. breast cancers is unknown. Recently, the authors have developed a culture method to grow two morphol. and antigenically distinguishable types of normal human breast epithelial cells (HBEC) derived from redn. mammoplasty. In this report, the authors studied the expression of ER in these two types of cells and their transformed cell lines. The results indicate that type I HBEC with luminal and stem cell characteristics expressed a variant ER (.apprx.48 kDa) by Western blot anal. This variant ER contains a deletion in the DNA binding domain (exon 2) as revealed by RT-PCR anal. The lack of the DNA-binding domain of the variant ER was also confirmed by the ER-estrogen responsive element binding assay, as well as by the immunofluorescence staining of the ER using anti-ER antibodies which recognize either the C-terminal or N-terminal region. In contrast, Type II HBEC with basal epithelial phenotype are ER-neg. Simian virus 40 (SV40) transformed Type I and Type II HBEC lines also expressed the variant ER. Tumors formed in athymic nude mice by in vitro transformed tumorigenic Type I cell lines, however, expressed a high level of wild type ER which was undetectable in these cells grown in vitro before and after tumor formation. Thus, there appears to be a differential ER mRNA splicing between the in vitro and in vivo milieu.
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
IT Exon (genetic element)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(2, splicing; expression of estrogen receptor splicing forms in normal human breast epithelial cell type with luminal and stem cell characteristics and **SV40** neoplastically transformed cell lines)

IT Protein motifs
(DNA-binding domain; expression of estrogen receptor splicing forms in normal human breast epithelial cell type with luminal and stem cell characteristics and **SV40** neoplastically transformed cell lines)
IT Breast **tumors**
Gene expression
Mammary epithelium
Simian virus 40
Transformation (neoplastic)
(expression of estrogen receptor splicing forms in normal human breast **epithelial cell** type with luminal and stem **cell** characteristics and **SV40** neoplastically transformed **cell** lines)
IT Estrogen receptors
RL: BOC (Biological occurrence); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(expression of estrogen receptor splicing forms in normal human breast epithelial cell type with luminal and stem cell characteristics and **SV40** neoplastically transformed cell lines)
IT Cyclin D1
p16INK4 protein
p21CIP1/WAF1 protein
p53 (protein)
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(expression of estrogen receptor splicing forms in normal human breast epithelial cell type with luminal and stem cell characteristics and **SV40** neoplastically transformed cell lines in relation to)
IT Splicing (RNA)
(messenger; expression of estrogen receptor splicing forms in normal human breast epithelial cell type with luminal and stem cell characteristics and **SV40** neoplastically transformed cell lines)
IT mRNA
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(pre-, splicing; expression of estrogen receptor splicing forms in normal human breast epithelial cell type with luminal and stem cell characteristics and **SV40** neoplastically transformed cell lines)

L21 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:46171 HCAPLUS
DOCUMENT NUMBER: 124:114038
TITLE: Mutational analysis of human papillomavirus type 16 E6
demonstrates that p53 degradation is necessary for **immortalization** of mammary epithelial cells
AUTHOR(S): Dalal, Sorab; Gao, Qingshen; Androphy, Elliot J.; Band, Vimla
CORPORATE SOURCE: Dep. Molecular Biol., Tufts Univ. School Medicine, Boston, MA, 02111, USA
SOURCE: J. Virol. (1996), 70(2), 683-8
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have previously demonstrated that normal human mammary

epithelial cells (MECs) are efficiently immortalized by human papillomavirus type 16 (HPV16) E6. HPV16 E6 binds to and induces p53 degrdn. in vitro and induces a marked redn. of p53 protein in MECs. Low-risk HPV6 E6 is defective for p53 binding and degrdn. in vitro but immortalized MECs at low efficiency. The HPV6 E6-immortalized MECs had markedly reduced levels of p53. To directly investigate whether the ability of HPV16 E6 to stimulate p53 degrdn. is required for E6-induced immortalization, a series of HPV16 E6 mutants were analyzed for the ability to bind and degrade p53 in vitro, induce a redn. in p53 levels in vivo, and immortalize MECs. The authors obsd. that one set of mutants efficiently immortalized MECs, caused a redn. in p53 levels in vivo, and degraded p53 in vitro. Other mutants immortalized MECs with low efficiency and either induced p53 degrdn. at low levels or were unable to induce p53 degrdn. in vitro; however, all of the immortal clones displayed low levels of p53. A third class of mutants did not immortalize MECs and failed to induce a redn. in p53 levels in vivo or degrade p53 in vitro. These results demonstrate that a redn. in p53 protein levels due to enhanced degrdn. is essential for MEC immortalization by HPV16 E6.

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 10

ST papillomavirus E6 oncoprotein p53 suppressor degrdn; mammary epithelium **immortalization** p53 suppressor papillomavirus

IT Molecular structure-biological activity relationship
(cell **immortalizing**; of human papilloma type 16 E6 oncoprotein)

IT Molecular association
(of human papilloma type 16 E6 oncoprotein with p53 **tumor** suppressor in relation to **immortalization** of mammary **epithelial cells**)

IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(E6, **human papillomavirus 16** E6 oncoprotein binding and induced degrdn. of p53 is necessary for **immortalization** of mammary epithelial cells)

IT Mammary gland
(epithelium, **human papillomavirus 16** E6 oncoprotein binding and induced degrdn. of p53 is necessary for **immortalization** of cells of)

IT Virus, animal
(human papilloma 16, E6 binding and induced degrdn. of p53 is necessary for **immortalization** of mammary epithelial cells)

IT Phosphoproteins
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BIOL (Biological study); PROC (Process)
(**tumor** suppressor, p53, **human papillomavirus 16** E6 oncoprotein binding and induced degrdn. of p53 is necessary for **immortalization** of mammary **epithelial cells**)

L21 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:862991 HCAPLUS
DOCUMENT NUMBER: 123:311815
TITLE: Characterization and response to **interleukin** 1 and **tumor** necrosis factor of

immortalized murine biliary **epithelial cells**

AUTHOR(S): Paradis, Khazal; Le, Oanh N. L.; Russo, Pierre; St-Cyr, Michel; Fournier, Helene; Bu, Dawen

CORPORATE SOURCE: Research Center, Sainte Justine Hospital, Montreal, Can.

SOURCE: Gastroenterology (1995), 109(4), 1308-15
CODEN: GASTAB; ISSN: 0016-5085

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Biliary epithelial cells are the target of numerous immune-mediated liver diseases, yet their role in pathogenesis remains unclear because of difficulties in obtaining pure prepns. The aim of this study was to establish pure clones of immortalized murine intrahepatic biliary epithelia cells. The transgenic mouse harboring the SV40 thermosensitive immortalizing mutant gene TsA58 under the control of the major histocompatibility complex class I promoter was used to establish conditionally immortalized intrahepatic bile duct cells by countercount centrifugal elutriation and clonal diln. Immortalized clones of cells expressing cytokeratin 19, which organized themselves into ductlike structures, were obtained. On electron-microscopic sections, cells were well differentiated and polarized. Cells proliferate in response to epidermal growth factor, interleukin 1.alpha., and tumor necrosis factor .alpha.. Using the reverse-transcriptase polymerase chain reaction technique, these cells were found to contain mRNA, which encodes for the interleukin 1 and tumor necrosis factor receptors. The availability of unlimited nos. of pure bile duct cells that behave in an identical fashion to biliary epithelial cells from "normal" mice will allow for more rigorous studies of the behavior and function of this epithelium.

CC 15-1 (Immunochemistry)
Section cross-reference(s): 9

ST **immortalization** biliary **epithelium** immunity liver disease; **interleukin** 1 **immortalized** biliary **epithelium cell**; **tumor** necrosis factor **immortalized** biliary **epithelium**

IT Immunity
Liver, disease
(establishment of **immortalized** murine biliary epithelial cells for study of immune-mediated liver diseases)

IT Biliary tract
(bile duct, epithelium, **immortalized** cells of; establishment of **immortalized** murine biliary epithelial cells for study of immune-mediated liver diseases)

IT Lymphokines and **Cytokines**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**interleukin** 1, responses of **immortalized** murine biliary **epithelial cells** to **interleukin** 1 and **tumor** necrosis factor)

IT Lymphokines and **Cytokines**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**tumor** necrosis factor, responses of **immortalized** murine biliary **epithelial cells** to **interleukin** 1 and **tumor** necrosis factor)

L21 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:479852 HCAPLUS
DOCUMENT NUMBER: 122:237633
TITLE: **Interleukin** 1.alpha. and **tumor** necrosis factor .alpha. stimulate autocrine amphiregulin expression and proliferation of human papillomavirus-**immortalized** and carcinoma-derived cervical **epithelial cells**
AUTHOR(S): Woodworth, Craig D.; McMullin, Erin; Iglesias, Maite; Plowman, Gregory D.
CORPORATE SOURCE: Lab. Biol., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1995), 92(7), 2840-4
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Infection with multiple sexually transmitted agents has been assocd. with inflammation of the cervix and an increased risk of cervical cancer in women infected with human papillomaviruses (HPVs). Two proinflammatory cytokines, interleukin 1.alpha. (IL-1.alpha.) and tumor necrosis factor .alpha. (TNF-.alpha.), inhibited proliferation of normal epithelial cells cultured from human cervix. In contrast, both cytokines significantly stimulated proliferation of cervical cell lines (5 of 7) immortalized by transfection with HPV-16 or -18 DNAs or lines derived from cervical carcinomas (7 of 11). Stimulation was dose dependent from 0.01 to 1.0 nM and was blocked by specific inhibitors, such as the IL-1 receptor antagonist or the TNF type 1 or 2 sol. receptors. Growth stimulation by IL-1.alpha. or TNF-.alpha. was accompanied by a 6-10-fold increase in RNA encoding amphiregulin, an epidermal growth factor (EGF) receptor ligand. Recombinant human amphiregulin (0.1 nM) was as effective as IL-1.alpha. or TNF-.alpha. in promoting proliferation. Monoclonal antibodies that blocked signal transduction by the EGF receptor or that neutralized amphiregulin activity prevented mitogenic stimulation by IL-1.alpha. or TNF-.alpha.. Thus, IL-1.alpha. and TNF-.alpha. stimulate proliferation of immortal and malignant cervical epithelial cells by an EGF receptor-dependent pathway requiring autocrine stimulation by amphiregulin. Furthermore, chronic inflammation and release of proinflammatory cytokines might provide a selective growth advantage for abnormal cervical cells in vivo.

CC 15-8 (Immunochemistry)
ST **cytokine** amphiregulin cervix epithelium; **interleukin** 1alpha amphiregulin cervix epithelium; tumor necrosis factor amphiregulin cervix epithelium
IT Signal transduction, biological
(in **interleukin** 1.alpha. and **tumor** necrosis factor .alpha. stimulation of amphiregulin expression and proliferation of carcinoma-derived cervical **epithelial cells**)
IT **Cell** proliferation
Epithelium
(**interleukin** 1.alpha. and **tumor** necrosis factor .alpha. stimulate amphiregulin expression and proliferation of carcinoma-derived cervical **epithelial cells**)
IT Uterus, neoplasm
(cervix, carcinoma, **interleukin** 1.alpha. and **tumor**

necrosis factor .alpha. stimulate amphiregulin expression and proliferation of carcinoma-derived cervical **epithelial cells**)

IT Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(epidermal growth factor/.alpha.-transforming growth factor, gene c-erbB, in **interleukin** 1.alpha. and **tumor** necrosis factor .alpha. stimulation of amphiregulin expression and proliferation of carcinoma-derived cervical **epithelial cells**)

IT Lymphokines and **Cytokines**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**interleukin** 1.alpha., **interleukin** 1.alpha. and **tumor** necrosis factor .alpha. stimulate amphiregulin expression and proliferation of carcinoma-derived cervical **epithelial cells**)

IT Lymphokines and **Cytokines**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**tumor** necrosis factor-.alpha., **interleukin** 1.alpha. and **tumor** necrosis factor .alpha. stimulate amphiregulin expression and proliferation of carcinoma-derived cervical **epithelial cells**)

IT Animal growth regulator receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.alpha.-transforming growth factor gene c-erbB, in **interleukin** 1.alpha. and **tumor** necrosis factor .alpha. stimulation of amphiregulin expression and proliferation of carcinoma-derived cervical **epithelial cells**)

IT 117147-70-3, Amphiregulin
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(**interleukin** 1.alpha. and **tumor** necrosis factor .alpha. stimulate amphiregulin expression and proliferation of carcinoma-derived cervical **epithelial cells**)

IT 62229-50-9, Epidermal growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptors; in **interleukin** 1.alpha. and **tumor** necrosis factor .alpha. stimulation of amphiregulin expression and proliferation of carcinoma-derived cervical **epithelial cells**)

L21 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:259649 HCAPLUS
DOCUMENT NUMBER: 122:29202
TITLE: **Immortalization** of subpopulations of respiratory epithelial cells from transgenic mice bearing **SV40** large T antigen
AUTHOR(S): Ikeda, Kazushige; Clark, Jean C.; Bachurski, Cindy J.; Wikenheiser, Kathryn A.; Cuppoletti, John; Mohanti, Sidhartha; Morris, Randal E.; Whitsett, Jeffrey A.
CORPORATE SOURCE: Children's Hospital Research Foundation, Children's Hospital Medical Center, Cincinnati, OH, 45229, USA

SOURCE: Am. J. Physiol. (1994), 267(3, Pt. 1), L309-L317
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Murine lung epithelial (MLE) cell lines were produced from lung tumors derived from transgenic mice bearing the viral oncogene, SV40 large T antigen, under transcriptional control of the promoter-enhancer region of the human surfactant protein C (SP-C) gene. Cells were selected on the basis of increased murine cystic fibrosis transmembrane conductance regulator (mCFTR) mRNA content and were diln. cloned to produce distinct immortalized epithelial cell lines. MLE-13a3 cell lines expressing high levels of mCFTR mRNA also expressed apolipoprotein J (apoJ) mRNA, a developmentally regulated glycoprotein expressed preferentially in fetal lung. SP-A, -B, and -C were not detected or were present at low levels in the MLE cells that contained abundant CFTR and apoJ mRNA. In contrast, MLE cells, cloned on the basis of abundant surfactant protein mRNAs, expressed apoJ and mCFTR mRNAs at low levels. Forskolin-stimulated short-circuit, typical of CFTR-mediated chloride transport activity, was generated by monolayers of subclones of the MLE-13a3 cell lines. Tumor necrosis factor-.alpha. stimulated mCFTR mRNA, whereas dexamethasone, retinoic acid, and phorbol ester had no effect on the levels of mCFTR mRNA in MLE-13a3 cells.

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 13
ST **immortalization** respiratory epithelium T antigen

IT Development, mammalian
Transformation, neoplastic
(**immortalization** of subpopulations of respiratory epithelial cells from transgenic mice bearing **SV40** large T antigen)

IT Ribonucleic acids, messenger
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);
BIOL (Biological study); OCCU (Occurrence)
(mCFTR; **immortalization** of subpopulations of respiratory epithelial cells from transgenic mice bearing **SV40** large T antigen)

IT Glycophosphoproteins
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);
BIOL (Biological study); OCCU (Occurrence)
(CFTR (cystic fibrosis transmembrane conductance regulator), **immortalization** of subpopulations of respiratory epithelial cells from transgenic mice bearing **SV40** large T antigen)

IT Lipoproteins
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(apo-, NA1, **immortalization** of subpopulations of respiratory epithelial cells from transgenic mice bearing **SV40** large T antigen)

IT Respiratory tract
(epithelium, **immortalization** of subpopulations of respiratory epithelial cells from transgenic mice bearing **SV40** large T antigen)

IT Antigens
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);

BIOL (Biological study); OCCU (Occurrence)
(large T, **immortalization** of subpopulations of respiratory epithelial cells from transgenic mice bearing **SV40** large T antigen)

IT Lymphokines and **Cytokines**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**tumor** necrosis factor-.alpha., **immortalization** of subpopulations of respiratory **epithelial cells** from transgenic mice bearing **SV40** large T antigen)

L21 ANSWER 23 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:554481 HCAPLUS
DOCUMENT NUMBER: 121:154481
TITLE: Enhanced proliferation, growth factor induction and **immortalization** by adenovirus **E1A** 12S in the absence of E1B
AUTHOR(S): Quinlan, Margaret P.
CORPORATE SOURCE: Dep. Microbiology Immunology, Univ. Tennessee, Memphis, TN, 38163, USA
SOURCE: Oncogene (1994), 9(9), 2639-47
CODEN: ONCNES; ISSN: 0950-9232
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Immortalization and transformation of primary epithelial cells requires expression of the adenovirus E1A and E1B genes, resp. The E1A gene is involved in growth stimulatory processes. Little is known about the mechanism utilized by E1B, however, roles in growth stimulatory processes have also been implied. To det. whether there are any functional interactions between E1A 12S and the E1B 55K and 19K polypeptides, primary epithelial cells were infected with 12S viruses with different E1B regions. In the absence of both E1B proteins, there was an increase in 12S expression. This resulted in increased levels of DNA synthesis, entry into S-phase of the cell cycle and increased levels of proliferation, in the presence or absence of serum. There was also a higher induction of growth factor activity. In the presence of the 55K and absence of the 19K protein, there was a decrease in 12S expression. However, the highest induction of proliferative responses was obsd. This suggests that expression of the 19K polypeptide inhibits 12S function directly. The lack of 19K expression also enabled the epithelial cells to have a much higher plating efficiency, achieve a greater cell d. and reach the immortalized state faster. Although some modest differences in p53 expression were obsd. when compared to mock, they could not be correlated with any phenotype.

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2

ST adenovirus **E1A** E1B gene epithelium transformation

IT Cell proliferation
(by epithelial cells, adenovirus gene **E1A** and E1B proteins in regulation of)

IT Transformation, neoplastic
(of epithelial cells, adenovirus gene **E1A** and E1B proteins in)

IT Epithelium

(proliferation and growth factor induction and **immortalization** of, adenovirus gene **E1A** and E1B proteins in)
IT Virus, animal
(adeno-, gene **E1A** and E1B proteins of, epithelial cell proliferation and growth factor induction and **immortalization** regulation by)
IT Animal growth regulators
RL: FORM (Formation, nonpreparative)
(epithelial cell growth factors, formation of, by epithelial cells, adenovirus gene **E1A** and E1B proteins effect on)
IT Phosphoproteins
RL: BIOL (Biological study)
(gene **E1A**, 171R (171 amino acid residues), in epithelial cell proliferation and growth factor induction and **immortalization**)
IT Phosphoproteins
RL: BIOL (Biological study)
(gene E1B, 176R (176 amino acid residues), in epithelial cell proliferation and growth factor induction and **immortalization**)
IT Proteins, specific or class
RL: BIOL (Biological study)
(gene E1B, 496R (496 amino acid residues), in epithelial cell proliferation and growth factor induction and **immortalization**)
IT Phosphoproteins
RL: BIOL (Biological study)
(**tumor** suppressor, p53, **epithelial cell** proliferation and growth factor induction and **immortalization** induction by adenovirus gene **E1A** and E1B proteins in relation to)

L21 ANSWER 24 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:72801 HCAPLUS
DOCUMENT NUMBER: 120:72801
TITLE: Production of immortalized distal respiratory **epithelial cell** lines from surfactant protein C/simian virus 40 large **tumor** antigen transgenic mice
AUTHOR(S): Wikenheiser, Kathryn A.; Vorbroker, Diane K.; Rice, Ward R.; Clark, Jean C.; Bachurski, Cindy J.; Oie, Herbert K.; Whitsett, Jeffrey A.
CORPORATE SOURCE: Med. Cent., Child. Hosp., Cincinnati, OH, 45229, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1993), 90(23), 11029-33
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Murine lung epithelial (MLE) cell lines representing the distal bronchiolar and alveolar epithelium were produced from lung tumors generated in transgenic mice harboring the viral oncogene simian virus 40 (SV40) large tumor antigen under transcriptional control of a promoter region from the human surfactant protein C (SP-C) gene. The cell lines exhibited rapid growth, lack of contact inhibition, and an epithelial cell morphol. for 30-40 passages in culture. Microvilli, cytoplasmic multivesicular bodies, and multilamellar inclusion bodies (morphol.

characteristics of alveolar type II cells) were detected in some of the MLE cell lines by electron microscopic anal. The MLE cells also maintained functional characteristics of distal respiratory epithelial cells including the expression of surfactant proteins and mRNAs and the ability to secrete phospholipids. Expression of the exogenous SV40 large tumor antigen gene was detected in all of the generated cell lines. The SP-C/SV40 large tumor antigen transgenic mice and the MLE cell lines will be useful for the study of pulmonary surfactant prodn. and regulation as well as lung development and tumorigenesis.

CC 9-11 (Biochemical Methods)
Section cross-reference(s): 3, 13, 14

ST lung cell line **SV40** T antigen; surfactant C lung cell line

IT Transformation, genetic
(by **SV40** large T antigen gene under contol of surfactant protein C gene promoter, of mouse, immortalized distal bronchiolar and alveolar epithelial cell lines derived from)

IT Gene, microbial
RL: BIOL (Biological study)
(for large T antigen of **SV40** virus, surfactant protein C gene promoter control of, in transgenic mouse, immortalized distal bronchiolar and alveolar epithelial cell lines derived from)

IT Lung
(alveolus, epithelium, immortalized cell line of distal, transgenic mouse bearing **SV40** large T antigen gene under control of surfactant protein C gene promoter as source of)

IT Bronchi
(bronchioles, epithelia, immortalized cell line of distal, transgenic mouse bearing **SV40** large T antigen gene under control of surfactant protein C gene promoter as source of)

IT Antigens
RL: BIOL (Biological study)
(large T, of **SV40** virus, gene for, surfactant protein C gene promoter control of, in transgenic mouse, immortalized distal bronchiolar and alveolar epithelial cell lines derived from)

IT Genetic element
RL: BIOL (Biological study)
(promoter, for surfactant protein C, **SV40** large T antigen gene controlled by, in transgenic mouse, immortalized distal bronchiolar and alveolar epithelial cell lines derived from)

IT Proteins, specific or class
RL: BIOL (Biological study)
(pulmonary surfactant-assocd., SP-C (surfactant protein C), gene promoter for, **SV40** large T antigen gene control by, in transgenic mouse, immortalized distal bronchiolar and alveolar epithelial cell lines derived from)

L21 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:406062 HCAPLUS
DOCUMENT NUMBER: 119:6062
TITLE: Human papillomavirus type 16 E6 gene cooperates with EJ-**ras** to **immortalize** primary mouse cells
AUTHOR(S): Storey, Alan; Banks, Lawrence
CORPORATE SOURCE: Int. Cent. Genet. Eng. Biotechnol., Trieste, I-34012, Italy
SOURCE: Oncogene (1993), 8(4), 919-24
CODEN: ONCNES; ISSN: 0950-9232

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human papillomaviruses (HPVs) are small DNA tumor viruses, a subset of which is closely assocd. with the development of cervical cancer. The viral E6 and E7 open reading frames encode multifunctional proteins that bind resp. to the p53 protein and to the product of the retinoblastoma tumor-suppressor gene. This study demonstrates that the HPV-16 E6 gene cooperates with EJ-ras to immortalize primary cultures of mouse kidney epithelial cells. HPV-16-immortalized cell lines expressing E6 but not E7
contained low levels of wild-type p53 protein. In contrast, those cells immortalized by EJ-ras alone contained elevated p53 protein levels, and were shown to contain a mutation in the gene. These results suggest that activating mutations in the p53 gene can functionally substitute for HPV-16 E6 in transforming primary cells.
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3
IT Transformation, neoplastic
(gene EJ-**ras** and human papillomavirus type 16 gene E6 regulation of, in kidney epithelial cells)
IT Mutation
(in gene p53, kidney epithelial cell transformation by gene EJ-**ras** and)
IT Kidney
(epithelium, human papillomavirus type 16 E6 gene and gene EJ-**ras** transformation of cells of)
IT Virus, animal
(human papilloma 16, E6 gene of, kidney epithelial cell transformation by gene EJ-**ras** and)
IT Antigens
RL: FORM (Formation, nonpreparative)
(p53 **tumor**, formation of, in human papillomavirus type 16 gene E6 and gene EJ-**ras** transformed kidney **epithelial cells**)
IT Gene, animal
RL: BIOL (Biological study)
(TP53, mutations in, kidney epithelial cells transformed by gene EJ-**ras** and)
IT Gene, microbial
RL: BIOL (Biological study)
(E6, of human papillomavirus type 16, kidney epithelial cell transformation by gene EJ-**ras** and)
IT Gene, animal
RL: BIOL (Biological study)
(c-Ha-**ras**, kidney epithelial cell transformation by human papillomavirus type 16 and)

L21 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1992:589778 HCAPLUS
DOCUMENT NUMBER: 117:189778
TITLE: Differential effects of the simian virus 40 early genes on mammary epithelial cell growth, morphology, and gene expression
AUTHOR(S): Wolff, Jacques; Wong, Connie; Cheng, Helen; Poyet, Patrick; Butel, Janet S.; Rosen, Jeffrey M.
CORPORATE SOURCE: Dep. Cell Biol., Baylor Coll. Med., Houston, TX, 77030-3498, USA

SOURCE: Exp. Cell Res. (1992), 202(1), 67-76
CODEN: ECREAL; ISSN: 0014-4827
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To study the effect of SV40 T-antigen in mammary epithelial cells, a rat .beta.-casein promoter-driven SV40 early-region construct was stably introduced into the clonal mouse mammary epithelial cell line HC11. With the expression of the viral T-antigens under the control of a hormone-inducible promoter, it was possible to dissoc. the effects of different levels of T-antigen expression on cell growth, morphol., and gene expression. Following hormonal induction, a rapid but transient induction of T-antigen was obsd., followed by a delayed induction of H4 histone mRNA. In T-antigen-pos. HC11 cells cultured in the absence of EGF, the expression of basal levels of T-antigen (in the absence of hormonal induction) led to a decreased doubling time and an increased cell d. In the presence of EGF, T-antigen expression resulted addnl. in an altered cell morphol. Despite the effects of T-antigen on cell growth and gene expression, the cells were unable to form colonies in soft agar and were nontumorigenic when transplanted into cleared mammary fat pads. They were, however, weakly tumorigenic in nude mice. Relatively high levels of p53 protein synthesis were obsd. in both the transfected HC11 cells and the parental COMMA-D cells, as compared to 3T3E fibroblasts and another mammary epithelial cell line. The HC11 and COMMA-D cells synthesized approx. equal levels of wild-type and mutated p53 proteins as defined by their reactivities with monoclonal antibodies PAb246 and PAb240, resp. Interactions between excess p53 and T-antigen may, in part, explain the failure of these cells to display a completely transformed phenotype.

CC 15-2 (Immunochemistry)
Section cross-reference(s): 14

ST **SV40** virus T antigen mammary epithelium; neoplasia **SV40** virus T antigen

IT Ribonucleic acids, messenger
RL: BIOL (Biological study)
(for H4 histone, **SV40** virus T antigen effect on expression of, in mammary epithelium)

IT Transformation, neoplastic
(in mammary epithelial cells, **SV40** virus T antigen in relation to)

IT Histones
RL: BIOL (Biological study)
(H4, mRNA for, **SV40** virus T antigen effect on expression of, in mammary epithelium)

IT Mammary gland
(epithelium, cell growth and morphol. and gene expression by, T antigen of **SV40** virus effect on)

IT Antigens
RL: BIOL (Biological study)
(large T, of **SV40** virus, mammary epithelial cells response to neoplastic transformation and protein p53 in relation to)

IT Antigens
RL: BIOL (Biological study)
(p53 **tumor**, expression of, by mammary **epithelial**

cells, **SV40** virus T antigen effect on, neoplastic transformation in relation to)

IT 50-23-7, Hydrocortisone 9002-62-4, Prolactin, biological studies 9004-10-8, Insulin, biological studies 62229-50-9, EGF
RL: BIOL (Biological study)
(T antigen of **SV40** virus expression in mammary epithelial cells in response to)

L21 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1992:405813 HCAPLUS
DOCUMENT NUMBER: 117:5813
TITLE: Release of **interleukin**-6 by human thyroid epithelial cells **immortalized** by simian virus 40 DNA transfection
AUTHOR(S): Kennedy, R. L.; Jones, T. H.; Davies, R.; Justice, S. K.; Lemoine, N. R.
CORPORATE SOURCE: Clin. Sci. Cent., Univ. Sheffield, Sheffield, S5 7AU, UK
SOURCE: J. Endocrinol. (1992), 133(3), 477-82
CODEN: JOENAK; ISSN: 0022-0795
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The factors which regulate interleukin-6 (IL-6) release from an immortalized human thyroid line (HTori3) were studied. IL-6 release over 24 h was stimulated by TSH (5000 .mu.U/mL), by forskolin (0.01 mmol/L), by fetal calf serum (1-20%) and by epidermal growth factor (20 ng/mL). Stimulation was also apparent with .gamma.-interferon and with tumor necrosis factor at concns. known to enhance class II major histocompatibility antigen expression by thyroid epithelium. The most potent factor tested was IL-1, which controls IL-6 release from other cell types. Threefold stimulation was found with 1 U/mL, rising to 350-fold with 1000 U/mL. The effect of IL-1 took 2 h to develop and was blocked by cycloheximide (100 .mu.mol/L). Stimulation was not markedly inhibited by pertussis toxin. Many of the actions of IL-1 are mediated by PGE2. At concns. as low as 30 nmol/L, PGE2 stimulated IL-6 release but the max. stimulation obtained with PGE2 was only 3-fold. The effect of IL-1 was not inhibited by indomethacin. These data provide further evidence that IL-6 is produced by human thyrocytes. The effect of IL-1 has not been demonstrated previously. Stimulation of IL-6 release by IL-1 did not appear to be mediated by prostaglandin. IL-6 may influence hormone release from the thyroid as it does in other tissues. High concns. of IL-6 in the thyroid may increase infiltration by, and activation of, lymphocytes in patients with autoimmune thyroid disease.

CC 15-5 (Immunochemistry)
ST **interleukin** 6 thyroid epithelium
IT Thyroid gland, metabolism
(epithelium, **interleukin**-6 release by human transformed cell line of, **cytokines** and growth factors effect on)
IT Lymphokines and **Cytokines**
RL: BIOL (Biological study)
(**interleukin** 1, **interleukin**-6 release by human transformed thyroid epithelium cell line stimulation by)
IT Lymphokines and **Cytokines**
RL: BIOL (Biological study)

(**interleukin** 6, release of, by human transformed thyroid epithelium cell line, **cytokines** and growth factors effect on)
IT Lymphokines and **Cytokines**
RL: BIOL (Biological study)
(**tumor** necrosis factor, **interleukin**-6 release by human transformed thyroid **epithelium cell** line stimulation by)
IT Interferons
RL: BIOL (Biological study)
(.gamma., **interleukin**-6 release by human transformed thyroid epithelium cell line stimulation by)
IT 9012-42-4, Adenylate cyclase
RL: BIOL (Biological study)
(in **interleukin**-6 release by human transformed thyroid epithelium cell line)
IT 9002-71-5, TSH 62229-50-9, Epidermal growth factor
RL: BIOL (Biological study)
(**interleukin**-6 release by human transformed thyroid epithelium cell line stimulation by)
IT 363-24-6, Prostaglandin E2
RL: BIOL (Biological study)
(**interleukin**-6 release by human transformed thyroid epithelium cell line stimulation by, **interleukin**-1 in relation to)

L21 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1991:406092 HCAPLUS
DOCUMENT NUMBER: 115:6092
TITLE: Efficient immortalization of luminal **epithelial cells** from human mammary gland by introduction of simian virus 40 large **tumor** antigen with a recombinant retrovirus
AUTHOR(S): Bartek, Jiri; Bartkova, Jirina; Kyprianou, Natasha; Lalani, El Nasir; Staskova, Zdenka; Shearer, Moira; Chang, Sidney; Taylor-Papadimitriou, Joyce
CORPORATE SOURCE: Imp. Cancer Res. Fund, London, WC2A 3PX, UK
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1991), 88(9), 3520-4
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB When defined in terms of markers for normal cell lineages, most invasive breast cancer cells correspond to the phenotype of the common luminal epithelial cell found in the terminal ductal lobular units. Luminal epithelial cells cultured from milk, which have limited proliferative potential, have now been immortalized by introducing the gene encoding simian virus 40 large tumor (T) antigen. Infection with a recombinant retrovirus proved to be 50-100 times more efficient than calcium phosphate transfection, and of the 17 cell lines isolated, only 5 passed through a crisis period as characterized by cessation of growth. When characterized by immunohistochem. staining with monoclonal antibodies, 14 lines showed features of luminal epithelial cells and of these, 7 resembled the common luminal epithelial cell type in the profile of keratins expressed. These cells express keratins 7, 8, 18, and 19 homogeneously and do not express keratin 14 or vimentin; a polymorphic epithelial mucin produced in vivo by

luminal cells is expressed heterogeneously and the pattern of fibronectin staining is punctate. Although the cell lines have a reduced requirement for added growth factors, they do not grow in agar or produce tumors in the nude mouse. When the v-Ha-ras oncogene was introduced into two of the cell lines by using a recombinant retrovirus, most of the selected clones senesced, but one entered crisis and emerged after 3 mo as a tumorigenic cell line.

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 10

IT Virus, animal
(**SV40**, large T antigen of, transfection of, human mammary gland luminal epithelium immortalization from, breast carcinogenesis study in relation to)

L21 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1990:92931 HCAPLUS
DOCUMENT NUMBER: 112:92931
TITLE: Cooperation of c-raf-1 and c-**myc** protooncogenes in the neoplastic transformation of simian virus 40 large **tumor** antigen-**immortalized** human bronchial **epithelial cells**
AUTHOR(S): Pfeifer, A. M. A.; Mark, G. E., III; Malan-Shibley, L.; Graziano, S.; Amstad, P.; Harris, C. C.
CORPORATE SOURCE: Lab. Hum. Carcinogenesis, Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1989), 86(24), 10075-9
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Overexpression of c-raf-1 and the myc family of protooncogenes is primarily assocd. with small cell carcinoma, which accounts for .apprx.25% of human lung cancer. To det. the functional significance of the c-raf-1 and/or c-myc gene expression in lung carcinogenesis and to delineate the relationship between protooncogene expression and tumor phenotype, both protooncogenes were introduced, alone or in combination, into human bronchial epithelial cells. Two retroviral recombinants, pZip-raf and pZip-myc, contg. the complete coding sequences of the human c-raf-1 and murine c-myc genes, resp., were constructed and transfected into simian virus 40 large tumor antigen-immortalized bronchial epithelial cells (BEAS-2B); this was followed by selection for G418 resistance. BEAS-2B cells expressing both the transfected c-raf-1 and c-myc sequences formed large cell carcinomas in athymic nude mice with a latency of 4-21 wk, whereas either pZip-raf- or pZip-myc-transfected cells were nontumorigenic after 12 mo. Cell lines established from tumors (designated RMT) revealed the presence of the cotransfected c-raf-1 and c-myc sequences and expressed morphol., chromosomal, and isoenzyme markers, which identified BEAS-2B cells as the progenitor line of the tumors. A significant increase in the mRNA levels of neuron-specific enolase was detected in BEAS-2B cells contg. both the c-raf-1 and c-myc genes and derived tumor cell lines. The data demonstrate that the concomitant expression of the c-raf and c-myc protooncogenes causes neoplastic transformation of human

bronchial epithelial cells resulting in large cell carcinomas with certain
neuroendocrine markers. The presented model system should be useful in studies of mol. events involved in multistage lung carcinogenesis.
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 14
IT Mouse
(gene c-**myc** of, gene c-raf-1 cooperation with, in **SV40** T antigen-**immortalized** human lung epithelial cell neoplastic transformation)
IT Transformation, neoplastic
(of **SV40** T antigen-**immortalized** human lung epithelial cells, gene c-raf-1 and c-**myc** cooperation in)
IT Animal cell line
(BEAS-2B, **SV40** T antigen-**immortalized** human lung epithelial, neoplastic transformation of, genes c-raf-1 and c-**myc** cooperation in)
IT Lung, neoplasm
(large-cell carcinoma, athymic mouse formation of, transfected genes c-raf-1 and c-**myc** cooperation in)
IT Gene and Genetic element, animal
RL: BIOL (Biological study)
(c-**myc**, gene c-raf-1 cooperation with, in **SV40** T antigen-**immortalized** human lung epithelial cell neoplastic transformation)
IT Gene and Genetic element, animal
RL: BIOL (Biological study)
(c-raf-1, gene c-**myc** cooperation with, in **SV40** T antigen-**immortalized** human lung epithelial cell neoplastic transformation)

L21 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1989:403665 HCAPLUS
DOCUMENT NUMBER: 111:3665
TITLE: Transfection of fetal rat intestinal epithelial cells by viral **oncogenes**: establishment and characterization of the **E1A-immortalized** SLC-11 cell line
AUTHOR(S): Emami, Shahin; Mir, Lluis; Gespach, Christian; Rosselin, Gabriel
CORPORATE SOURCE: Inst. Natl. Sante Rech. Med., Hop. Saint-Antoine, Paris, 75571, Fr.
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1989), 86(9), 3194-8
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Intestinal epithelial cells from 19-day-old rat fetuses underwent electropermeabilization and were successfully transfected by three recombinant plasmids contg. the cloned oncogenes from the human adenovirus
type 2 early region E1A (SLC-11 cells) and polyoma virus and simian virus 40 large T tumor antigens (SlC-21 and SLC-41 cells). SLC-11 cells were propagated for 21 mo in culture (current passage, 76; doubling time, 17 h)
and were immortalized by E1A, as shown by RNA transfer blot (Northern blot) anal. and indirect immunofluorescence of the nuclear oncoproteins. These cells were not tumorigenic in either athymic nude mice or syngeneic

Wistar rats and showed a nearly normal karyotype with minimal chromosomal changes. The immortalized epithelial cell line SLC-11 retained several of the phenotypes obsd. in the parent cells of the intestinal mucosa, including cytoplasmic villin, cytokeratins, enkephalinase, and cell surface receptors sensitive to vasoactive intestinal peptide. Apparently, immortal SLC-11 cells are a suitable model for studying the proliferation and differentiation of epithelial intestinal cells and analyzing cancer progression in the gastrointestinal tract.

CC 9-11 (Biochemical Methods)
Section cross-reference(s): 3, 13, 14

ST transfection intestine epithelium virus **oncogene**; SLC11 cell line **immortalization**

IT Gene and Genetic element, microbial
RL: ANST (Analytical study)
(for large T **tumor** antigens, intestine **epithelium cells** transfection by)

IT Transformation, genetic
(of intestine epithelium cells, by viral **oncogenes**)

IT Animal cell line
(SLC-11, **immortalization** of, transfection of intestine epithelium cells by viral **oncogenes** in)

IT Virus, animal
(**SV40**, **oncogenes** of, intestine epithelium cells transfection by)

IT Virus, animal
(adenovirus 2, **oncogenes** of, intestine epithelium cells transfection by)

IT Intestine
(epithelium, transfection of cells of, by viral **oncogenes** for cell line **immortalization**)

IT Embryo
(fetus, transfection of intestine epithelium cells of, by viral **oncogenes**)

IT Virus, animal
(polyoma-, **oncogenes** of, intestine epithelium cells transfection by)

IT Gene and Genetic element, microbial
RL: ANST (Analytical study)
(**E1A**, intestine epithelium cells transfection by)

L21 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1988:183568 HCAPLUS
DOCUMENT NUMBER: 108:183568
TITLE: Transformation of human bronchial epithelial cells by infection with **SV40** or adenovirus-12 **SV40** hybrid virus, or transfection via strontium phosphate coprecipitation with a plasmid containing **SV40** early region genes
AUTHOR(S): Reddel, Roger R.; Ke, Yang; Gerwin, Brenda I.; McMenamin, Mary G.; Lechner, John F.; Su, Robert T.; Brash, Douglas E.; Park, Joo Bae; Rhim, Johng S.; Harris, Curtis C.
CORPORATE SOURCE: Lab. Hum. Carcinogenesis, Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: Cancer Res. (1988), 48(7), 1904-9

CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Normal human bronchial epithelial cells were infected with SV40 virus or an adenovirus 12-SV40 hybrid virus or transfected via strontium phosphate copptn. with plasmids contg. the SV40 early region genes. Colonies of morphol. altered cells were isolated and cultured; these cells had extended culture lifespans compared to normal human bronchial epithelial cells. All cultures eventually underwent senescence, with the exception of one which appears to have unlimited proliferative potential. Colonies arising after viral infection were screened for virus prodn. by cocultivation with Vero cells; only viral nonproducer cultures were analyzed further. The cells retained electron microscopic features of epithelial cells, and keratin and SV40 T-antigen were detected by indirect immunofluroescence. All of the cultures were aneuploid with karyotypic abnormalities characteristic of SV40-transformed cells. No tumors formed after s.c. injection of the cells in nude mice. These cells should be useful for studies of multistage bronchial epithelial carcinogenesis.
CC 10-6 (Microbial Biochemistry)
Section cross-reference(s): 3
ST bronchus epithelium transformation **SV40** adenovirus gene
IT Transformation, neoplastic
(of human bronchial **epithelial cells**, by DNA **tumor** virus genes)
IT Virus, animal
(**SV40**, transformation of human cells by early genes of)
IT Virus, animal
(adenovirus 12, **SV40** hybrid with, transformation of human cells by)
IT Gene and Genetic element, microbial
RL: BIOL (Biological study)
(early, of **SV40** virus, in transformation of human bronchial epithelial cells)
IT Bronchi
(**epithelia**, transformation of **cells** from human, by DNA **tumor** virus genes)

L21 ANSWER 32 OF 32 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1986:607030 HCAPLUS
DOCUMENT NUMBER: 105:207030
TITLE: Fluctuation of simian virus 40 (**SV40**) super T-antigen expression in **tumors** induced by **SV40**-transformed mouse mammary **epithelial cells**
AUTHOR(S): Butel, Janet S.; Wong, Connie; Evans, Bradley K.
CORPORATE SOURCE: Dep. Virol., Baylor Coll. Med., Houston, TX, 77030, USA
SOURCE: J. Virol. (1986), 60(2), 817-21
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Higher-mol.-wt. forms of the simian virus 40 (SV40) large tumor antigen (T-Ag), designated super T-Ag, are commonly found in SV40-transformed rodent cells. The potential role of super T-Ag in neoplastic progression was examd. by using a series of clonal SV40-transformed mouse mammary epithelial cell lines. An assocn. between the presence of super T-Ag and

cellular anchorage-independent growth in methylcellulose was confirmed. However, tumorigenicity in nude mice did not correlate with the expression of super T-Ag. In the tumors that developed in nude mice, super T-Ag expression fluctuated almost randomly. Cell surface iodination showed that super T-Ag mols. were transported to the epithelial cell surface. The biol. functions of super T-Ag remain obscure, but it is clear that it is not important for tumorigenicity by SV40-transformed mouse mammary epithelial cells. Super T-Ag may be most important as a marker of genomic rearrangements by the resident viral genes in transformed cells.

CC 14-1 (Mammalian Pathological Biochemistry)

ST **SV40** virus super T antigen tumor; neoplastic transformation
SV40 super T antigen

IT Transformation, neoplastic
(by **SV40** virus, super T-antigen expression fluctuation in, tumorigenic activity in relation to)

IT Virus, animal
(**SV40**, super T-antigen of, expression of, fluctuation of, in virus-transformed cells, tumorigenic activity in relation to)

IT Antigens
RL: BIOL (Biological study)
(super T, of **SV40** virus, expression of, fluctuation of, in virus-transformed cells, tumorigenic activity in relation to)

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L1            49 S EPITHEL? (3A) (TUMOR# OR TUMOUR) (2A) CELL#
L2             2 S L1 AND IMMORTALI?
L3             2 S L1 AND ONCOGEN?
L4           233 S EPITHEL? (S) (TUMOR# OR TUMOUR) (S) CELL#
L5             5 S L4 AND IMMORTALI?
L6             9 S L4 AND ONCOGEN?
L7          2621 S BONE MARROW
L8            16 S L4 AND L7
L9            13 S L2 OR L3 OR L5 OR L6
L10            1 S L9 AND L7
L11            4 S L1 AND L7
L12            0 S L1 AND SV40
L13            0 S L1 AND LARGE T ANTIGEN?
L14         1611 S RAS OR WT1 OR BCL 2 OR P53MUT OR MYC OR HER 2 NEU OR HPV 16
O
L15            0 S L1 AND L14
L16         1367 S IMMUNOSTIM? OR IMMUNO STIMUL?
L17            0 S L1 AND L16
L18         6779 S B7 OR CYTOKINE# OR IL (W) (2 OR L4 OR L7) OR INTERLEUKIN#
OR
L19            2 S L18 AND L1
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L20  ANSWER 1 OF 9  WPIDS COPYRIGHT 2000   DERWENT INFORMATION LTD
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AN 1999-551132 [46] WPIDS
DNC C1999-160792
TI Producer cells infected with oncolytic viruses.
DC B04 D16
IN ALBELDA, S M; CAPARRELLI, D J; COUKOS, G; KAISER, L R; MOLNAR-KIMBER, K L
PA (UYPE-N) UNIV PENNSYLVANIA
CYC 22
PI WO 9945783 A1 19990916 (199946)* EN 51p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
ADT WO 9945783 A1 WO 1999-US5466 19990312
PRAI US 1998-77681 19980312
AB WO 9945783 A UPAB: 19991110
NOVELTY - A producer cell line (I) infected with oncolytic viruses capable of replication in the producer cell, is new. (I) is incapable of sustained survival within the body and may be administered to cancer patients to kill tumor cells.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method (A) of treating cancers by administering a mammalian (I); and

(2) an anti-tumor agent comprising a mammalian cell containing thymidine kinase incapable of sustained survival in the human body and which exhibits binding affinity for a tumor cell. The mammalian cell metabolizes gancyclovir upon its administration, to generate a cytotoxic metabolite to the tumor cell to which the mammalian cell has bound.

ACTIVITY - Cytostatic; anti-cancer.

MECHANISM OF ACTION - The producer cell binds to tumor cells and lyses releasing the viruses which then infect and kill the tumor cells. The producer may also transfer cytotoxic chemicals (such as those produced by the metabolism of Gancyclovir) to the tumor cell increasing its effectiveness.

USE - The producer **cell** is used in the manufacture of a medicament for administration to a patient to kill **epithelial tumor cells**, especially **epithelial** ovarian cancer **cells**,

ADVANTAGE - The oncolytic virus replicates in (and kills) tumor cells but not in normal cells.

Dwg.0/0

L20 ANSWER 2 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-034723 [03] WPIDS
DNC C1999-010478
TI New nucleic acid encoding secreted polypeptide zsig15 - used as a marker for tumour cells, useful for diagnosis and treatment of cancers, inflammation and hyperplasia.
DC B04 D16
IN GROSSMANN, A; SHEPPARD, P O
PA (ZYMO) ZYMOGENETICS INC
CYC 77
PI WO 9850552 A1 19981112 (199903)* EN 99p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW
MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN ZW
AU 9874801 A 19981127 (199915)
ADT WO 9850552 A1 WO 1998-US9584 19980506; AU 9874801 A AU 1998-74801 19980506
FDT AU 9874801 A Based on WO 9850552
PRAI US 1997-45703 19970506
AB WO 9850552 A UPAB: 19990122
New isolated nucleic acid (I): (a) is part of a 1733 bp sequence (S1), extending from nucleotide (nt) 97 to 1215; (b) is an orthologue of (a); (c) is an allelic variant of (a) or (b); (d) is a sequence that encodes a polypeptide at least 80% identical with the amino acid (aa) region 22-394 of a 437 aa sequence (S2) (given in the specification), or (e) is a degenerate version of (a)-(d). Also new are: (A) isolated nucleic acid (Ia) containing nt 97-582, 655-1215 or 655-1344 of (S1); (B) isolated nucleic acid (Ib) encoding a fusion protein of two polypeptides encoded by nt 97-582 and nt 655-1215 of (S1); (C) expression vectors containing (I); (D) cultured cells carrying this vector; (E) polypeptides (II) that contain aa 22-394 of (S2), also its orthologues, allelic variants and peptides with at least 80% identity; (F) polypeptides (IIa) containing aa 22-183, 208-394 or 208-437 of (S2); (G) fusion peptide containing aa 22-183 and 208-394 of (S2); (H) antibodies (Ab) specific for an epitope in (S2), and (I) oligonucleotide probes and primers containing at least 14 consecutive nt from the nt 34-1344 region of (S1).

USE - Cells of (D) are used to produce recombinant polypeptides. (I) encodes a secreted polypeptide, designated zsig15, which is a marker for differentiation in normal and **tumour cells** (particularly **epithelial cells** and derived tumours of colon, breast and prostate). zsig15 can be used to raise Ab; as cell culture additive to replace serum; for specific promotion of growth and development of epithelial cells; to identify specific (ant)agonists, also where conjugated to a toxin, to deliver these to cells expressing the cognate receptor (e.g. to kill cells of blood, colon, breast and **bone marrow** cancers), and to identify/isolate receptors involved in cancer metastases. Antagonists of zsig15 (e.g. Ab, soluble receptors, ribozymes) are used to characterise sites of ligand/receptor interaction, and to inhibit zsig15 activity in vivo or in vitro. Ab, or other binding proteins, are used to tag cells, for affinity purification, for delivering toxins, drugs etc. to zsig15-expressing cells (especially tumours), for screening expression libraries, in diagnostic assays for zsig15, and to raise anti-idiotypic antibodies. (I), (II) and Ab are used to treat, prevent and diagnose inflammation and hyperplastic conditions other than tumours, e.g. (I) is used in gene or antisense therapy. Fragments of (I) are used as probes to detect mutations on chromosome 19 and for generating transgenic animals.
Dwg.0/0

L20 ANSWER 3 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-584374 [50] WPIDS
DNC C1998-175035
TI Oligonucleotide primers for amplifying cytokeratin 18 cDNA - especially for detecting metastatic **epithelial tumour cells**.

DC B04 D16
IN NEUMAIER, M; TSCHENTSCHER, P; WAGENER, C
PA (WAGE-I) WAGENER C
CYC 1
PI DE 19716346 C1 19981119 (199850)* 9p
ADT DE 19716346 C1 DE 1997-19716346 19970418
PRAI DE 1997-19716346 19970418
AB DE 19716346 C UPAB: 19981223
Oligonucleotides having the following sequences are new:
5'-TGCTCACCACACAGTCTGAT-3', 5'-CACTTTGCCATCCACTAGCC-3',
5'-TGGAGGACCGCTACGCCCTA-3' and 5'-CCAAGGCATCACCAAGACTA-3'.
USE - The oligonucleotides are useful as primers in an assay for detecting the cytokeratin 18 (CK18) gene in a sample, especially an organ (e.g. **bone-marrow**) smear, puncture or biopsy sample or a blood, sputum, urine, stool, liquor, bile, lymph or gastrointestinal secretion sample, comprising isolating mRNA from the sample, reverse-transcribing the mRNA into cDNA, amplifying the cDNA by PCR using the primers, and detecting the amplified cDNA. The assay can be used to detect epithelial cells, especially metastases of **tumour cells** of **epithelial** origin.
ADVANTAGE - The primers have higher affinity for CK18 cDNA than for processed CK18 pseudogenes. The detection limit of the assay is 1-10 epithelial cells per ml blood.
Dwg.0/4

L20 ANSWER 4 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-286977 [25] WPIDS
DNC C1998-089008
TI Antisense oligonucleotides that down regulate the erbB-2 **oncogene** - useful to inhibit ERBB2 tyrosine kinase receptor expression in cancer cells to treat epithelial cell, breast, ovarian, lung or colon cancer.
DC B04 D16
IN INGLEHART, J D; MARKS, J R; VAUGHN, J P
PA (UYDU-N) UNIV DUKE
CYC 21
PI WO 9820168 A1 19980514 (199825)* EN 31p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9852594 A 19980529 (199841)
US 5910583 A 19990608 (199930)
ADT WO 9820168 A1 WO 1997-US20910 19971103; AU 9852594 A AU 1998-52594 19971103; US 5910583 A US 1996-740821 19961104
FDT AU 9852594 A Based on WO 9820168
PRAI US 1996-740821 19961104
AB WO 9820168 A UPAB: 19980624
Antisense oligonucleotides that down regulate the erbB-2 **oncogene** with sequence (I) ('US-3') or (II) ('UT-1') are new. GGTGCTCACTGCGGC (I) TGCGGCTCCGGCCCC (II)
USE - The oligonucleotides are useful as antisense oligonucleotides for inhibiting the expression of the ERBB2 tyrosine kinase receptor in a cell, in vitro or in vivo (claimed); such cells may be e.g. **epithelial** or **tumour cells**, especially breast cancer, ovarian cancer, lung cancer and colon cancer cells (claimed). The oligonucleotides are useful in vivo to treat cancer (especially epithelial cell, breast, ovarian, lung or colon cancer) in a human or other animal,

especially when the cancer is characterised by cells that overexpress the ERBB2 tyrosine kinase receptor and the oligonucleotides are administered intravenously (claimed). In vitro, they may be used in a prior art process to identify compounds that inhibit the overexpression of the ERBB2
tyrosine kinase receptor. The oligonucleotides can also be included in pharmaceutical compositions with an acceptable carrier (claimed) e.g. for therapeutic administration. The antisense oligonucleotides are targeted to the erbB-2 **oncogene** since this is overproduced in a high proportion of breast and other epithelial cancers, but shows low expression in most normal adult tissues, making it an attractive therapeutic target. The oligonucleotides may also be labelled with a suitable detectable group (e.g. a radioisotope) and used as hybridisation probes to detect the ERBB2 gene, or the molecular weights of the oligonucleotides determined and the oligonucleotides used as molecular weight markers.
Dwg.0/5

L20 ANSWER 5 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-202244 [18] WPIDS
DNC C1997-064737
TI Tissue regeneration methods - use mesenchymal cells to induce differentiation in terminally differentiated adult tissues.
DC B04 D16
IN CUNHA, G R; LIPSCHUTZ, J H; YOUNG, P F
PA (REGC) UNIV CALIFORNIA
CYC 73
PI WO 9710348 A1 19970320 (199718)* EN 40p
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
AU 9672387 A 19970401 (199730)
ADT WO 9710348 A1 WO 1996-US14781 19960913; AU 9672387 A AU 1996-72387 19960913
FDT AU 9672387 A Based on WO 9710348
PRAI US 1995-3735 19950914
AB WO 9710348 A UPAB: 19970502
A new method (M1) of producing a differential cell with a selected phenotype comprises: (a) contacting a mesenchymal cell with a 2nd cell; and (b) incubating the mesenchymal cell (in vitro or in vivo) with the 2nd
cell so as to induce the 2nd cell to produce a differentiated cell with a selected phenotype. Also claimed are: (1) a method (M2) for producing a selected cell from a terminally differentiated cell comprising incubating the terminally differentiated cell with a mesenchymal cell; (2) a cell (pref. present in a mammal) produced by incubating a terminally differentiated cell with an embryonic cell; and (3) a mesenchymal-epithelial tissue recombinant which is a host animal of a first species comprising a mesenchymal cell from a 2nd species and an epithelial cell from a 3rd species.

In M1 the 2nd **cell** is esp. **epithelial** and from a **tumour** or is **immortalised**. The mesenchymal cell and epithelial cell are from different species and may be from the same or different organ(s). In both M1 and M2, a plurality of (terminally) differentiated cells are produced which form amino acid epithelial tissue

which may be kidney, pancreatic, bladder, lung intestinal, liver, prostate or reproductive epithelium. Esp. in M2, the terminally differentiated cell is a ureter cell and the selected cell is a kidney cell.

USE - The methods use permissive or instructive induction to induce selected cell types in an animal. Direct implantation of mesenchymal tissue into suitably prepd. sites of an adult animal results in new functional organs in situ by induction of adult epithelial cells.

ADVANTAGE - The methods are used in place of organ transplant in patient with chronic or irreversible organ failure. The host animals are useful as animal models, in partic. for the study of cancer and methods for reducing tumourigenicity. Kits are provided.

Dwg.0/2

L20 ANSWER 6 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-087373 [08] WPIDS
DNN N1997-071901 DNC C1997-028474
TI New **immortalised epithelial tumour cells** - having **immortalising oncogene** introduced into genome(s) or another replicating genetic element.
DC B04 D16 S03
IN DICKMANNS, A; FANNING, E; PANTEL, K; RIETHMULLER, G; RIETHMUELLER, G
PA (MICR-N) MICROMET GMBH
CYC 72
PI WO 9700946 A1 19970109 (199708)* EN 47p
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AU AZ BB BG BR BY CA CN CZ EE GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LV MD MG MK MN MW MX NO NZ PL RO RU SD SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9664153 A 19970122 (199719)
NO 9706036 A 19980203 (199816)
EP 839183 A1 19980506 (199822) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 11507834 W 19990713 (199938) 44p
ADT WO 9700946 A1 WO 1996-EP2747 19960624; AU 9664153 A AU 1996-64153 19960624; NO 9706036 A WO 1996-EP2747 19960624, NO 1997-6036 19971222; EP 839183 A1 EP 1996-923904 19960624, WO 1996-EP2747 19960624; JP 11507834 W WO 1996-EP2747 19960624, JP 1997-503590 19960624
FDT AU 9664153 A Based on WO 9700946; EP 839183 A1 Based on WO 9700946; JP 11507834 W Based on WO 9700946
PRAI EP 1995-109860 19950623
AB WO 9700946 A UPAB: 19970220

Epithelial tumour cell (ETC) with metastatic potential comprises integrated in its genome or another replicative genetic element an externally introduced **immortalising oncogene** which is expressed in the cell.

Also claimed is an antibody or fragment or deriv. of the antibody or fragment which specifically recognises a tumour cell such as ETC.

USE - The ETC or antibody can be used for the prophylaxis and/or treatment of cancer and/or cancer metastasis. They can also be used for the prepn. of tumour vaccines. They can also be used in diagnostic compsns. The ETC can also be used for the ex vivo stimulation of a patient's immune cells. The cells are used in pharmaceutical and diagnostic compsn. (all claimed).

ADVANTAGE - The ETCs provide for the specific and unlimited expansion

of **tumour cells** of **epithelial** origin with metastatic potential.
Dwg.0/5

L20 ANSWER 7 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1996-433540 [43] WPIDS
DNC C1996-136035
TI Selective sodium-proton anti-porter inhibiting medicaments - contg. halocin H7, used e.g. as diuretics, antihypertensives, anti-ischaemic agents and cell growth inhibitors.
DC B04 D16
IN ALBA, CARBALLO I; COLOM, VALIENTE F; MESEGUER, SORIA I; SORIA, ESCOMS B; TORREBLANCA, CALVO M
PA (UYAL-N) UNIV ALICANTE
CYC 20
PI WO 9628179 A1 19960919 (199643)* EN 17p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
ES 2094696 A1 19970116 (199710)
ES 2094696 B1 19970901 (199742)
ADT WO 9628179 A1 WO 1996-ES48 19960306; ES 2094696 A1 ES 1995-468 19950309; ES 2094696 B1 ES 1995-468 19950309
PRAI ES 1995-468 19950309
AB WO 9628179 A UPAB: 19961025
The use of halocin H7 (I) is claimed for prodn. of the following medicaments: diuretics and antihypertensives; protectants against cardiac and nervous ischaemia; insulin resistance reducing agents; inhibitors of hydrochloric acid formation in the gastric mucosa; cell growth inhibitors;
cell vol. regulators; bacterial and microbial growth regulators, and epithelial transport inhibitors.
USE - (I) is an antibiotic which specifically inhibits the sodium-protein (Na+/H+) anti-porter (SPA) in the cellular membrane. SPA is
involved in many cellular processes (e.g. control of cellular pH, Na+ concn., vol. and division) and participates in numerous hypertension, cardiac and cerebral ischaemia, **tumour cell** division, **epithelial** transport, macrophage activation, **cytokine** release. immunosuppression (e.g. transplants, autoimmunity), essential hypertension, insulin resistance (in non-insulin dependent diabetes) and cytotoxicity during myocardial reperfusion.
ADVANTAGE - (I) inhibits SPA selectively and thus has markedly reduced side-effects compared with amiloride and its derivs. (which inhibit SPA non-specifically). (I) is a naturally produced and metabolised
protein, which inhibits SPA specifically at low concns. (reducing side-effects). (I) is effective over a wide range of salt concns., temp. and pH and is resistant to trypsin (allowing use in the gastro-intestinal tract). Since (I) is sensitive to pronase, its effect can be terminated when required.
Dwg.0/0

L20 ANSWER 8 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1990-077202 [11] WPIDS
CR 1987-293113 [42]; 1987-306747 [43]; 1990-115985 [15]; 1995-381883 [49];
1996-040229 [04]; 1996-221250 [22]; 1997-065136 [06]; 1997-258218 [23];

1999-069746 [06]
DNC C1990-033773
TI Matrices for cell cultures - comprising stromal cells on three-dimensional matrix.
DC A89 A96 B04 D16 P31 S03
IN NAUGHTON, B A; NAUGHTON, G K
PA (ADTI-N) ADVANCED TISSUE SCI INC; (MARR-N) MARROW-TECH INC
CYC 19
PI EP 358506 A 19900314 (199011)* EN 70p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
ZA 8906886 A 19900627 (199031)
US 4963489 A 19901016 (199044) 29p
JP 04501657 W 19920326 (199219) 56p
AU 644578 B 19931216 (199406)
CA 1335657 C 19950523 (199528)
IL 91536 A 19961031 (199704)
ADT EP 358506 A EP 1989-309085 19890907; ZA 8906886 A ZA 1989-6886 19890908; US 4963489 A US 1988-242096 19880908; JP 04501657 W JP 1989-509402 19890907; AU 644578 B AU 1989-42114 19890907, Div ex AU 1987-73568 ; CA 1335657 C CA 1989-610617 19890907; IL 91536 A IL 1989-91536 19890906
FDT AU 644578 B Previous Publ. AU 8942114, Based on WO 9002796
PRAI US 1988-242096 19880908; US 1986-853569 19860418; US 1987-36154 19870403; US 1987-38110 19870414; US 1989-402104 19890901
AB EP 358506 A UPAB: 19990316
New 3-dimensional stromal matrices comprise subconfluent stromal cells on a 3-dimensional matrix whose material compsn. and shape allows cells to attach to it or can be modified to allow cells to attack to it, and which allows cells to grow in more than one layer.
USE - The matrices are useful as substrates for culturing parenchymal cells esp. (a) hematopoietic cells for prodn. of **bone marrow** cultures for transplantation, (b) melanocytes and keratinocytes for prodn. of skin cultures e.g. for use as skin grafts, (c) neuronal cells and astrocytes for prodn. of cultures modelling the blood-brain barrier, (d) mucosal **epithelial cells**, (e) **tumour cells**, e.g. for malignancy diagnosis, (f) hepatocytes for prodn. of liver cell cultures or (g) endocrine acinar cells for prodn. of pancreatic cultures (N.B. in cases (c) and (d) the stromal cells are confluent, and in case (b) the stromal cells may be confluent or subconfluent). The various cultures may also be used for cytotoxicity testing of substances in vitro. Genetically transformed parenchymal cells may also be cultured.
Dwg.0/25

L20 ANSWER 9 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1984-160078 [26] WPIDS
DNN N1984-119045 DNC C1984-067510
TI Antibody reactive with human tumour cell lines - useful in diagnosis and treatment of cancer esp. of breast.
DC B04 D16 S03
PA (LUDW-N) LUDWIG INST CANCER RES; (RESE) RESEARCH CORP
CYC 13
PI EP 112093 A 19840627 (198426)* EN 45p
R: AT BE CH DE FR GB IT LI LU NL SE
GB 2131830 A 19840627 (198426)

US 4731238 A 19880315 (198814)
CA 1276119 C 19901113 (199051)
US 5003046 A 19910326 (199115)
ADT EP 112093 A EP 1983-307300 19831130; GB 2131830 A GB 1982-35216 19821210; US 4731238 A US 1983-558538 19831205; US 5003046 A US 1987-137037 19871223
PRAI GB 1982-35216 19821210
AB EP 112093 A UPAB: 19930925
Antibody reactive with MCF-7, EJ, Baron, ZR and Papiou human tumour cell lines, and human breast carcinomas, and non-reactive with lymphocytes and colony-forming units of **bone marrow**.

Monoclonal lymphocyte hybridoma as a biologically pure culture capable of expressing an antibody as defined above is new. It is esp. a culture of hybridoma LICR-LON Fib 75 (CNCM I-22). Antigen binding to the antibody defined above is new.

The antibody is useful for the therapeutic treatment and diagnosis of breast cancer and other cancers, esp. for the accurate staging of the cancer so that approp. therapy can be designed. Latent metastases may be detected. The monoclonal antibody does not react with colony-forming units of normal human **bone marrow** but has specific cytotoxicity to a no. of human **epithelial tumour cell** lines. It may be conjugated to ricin or a toxin or used in association with complement, esp. for aiding autologous **bone marrow** grafting, e.g. with breast and oat cell carcinoma.
0/0

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     (FILE 'BIOSIS' ENTERED AT 10:54:15 ON 13 JAN 2000)
               DEL HIS Y
L1          1057 S EPITHELI? (3A) (TUMOR OR TUMOUR) (2W) CELL#
L2          6573 S IMMORTALI?
L3         41098 S ONCOGEN?
L4            14 S L1 AND L2
L5            36 S L1 AND L3
L6             2 S L4 AND L5
L7          8466 S  SV40
L8             0 S L1 AND L8\7
L9             5 S L1 AND L7
L10        40750 S  HIS
L11        34414 S RAS OR WT1 OR BCL 2 OR P53MUT OR HER 2 NEU OR HPV (2W) (16
OR
L12           42 S L1 AND L11
L13            8 S L12 AND (L2 OR L3)
L14         6124 S  IMMUNOSTIM? OR IMMUNO STIMUL?
L15            2 S L14 AND L1
L16       164307 S B7 OR CYTOKINE# OR IL (2W) (2 OR 4 OR 7) OR INTERLEUKIN# OR
I
L17           53 S L1 AND L16
L18            2 S L17 AND (L2 OR L3 OR L11)
L19           17 S L6 OR L9 OR L13 OR L15 OR L18

     FILE 'BIOSIS' ENTERED AT 11:02:19 ON 13 JAN 2000

=> d bib ab st 1-17


L19  ANSWER 1 OF 17  BIOSIS  COPYRIGHT 2000 BIOSIS
AN   1999:484705  BIOSIS
DN   PREV199900484705
TI   Generation of protective immunity against an immunogenic carcinoma
     requires CD40/CD40L and B7/CD28 interactions but not CD4+ T cells.
AU   Eck, Steven C.; Turka, Laurence A. (1)
CS   (1) Department of Medicine, University of Pennsylvania, 422 Curie
     Boulevard, 901 Stellar-Chance Laboratories, Philadelphia, PA, 19104-6100
     USA
SO   Cancer Immunology Immunotherapy, (Sept., 1999) Vol. 48, No. 6, pp.
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336-341.
ISSN: 0340-7004.
DT Article
LA English
SL English
AB Interactions between CD40 and CD40L play a central role in the regulation of both humoral and cellular immunity. Recently, interactions between these molecules have also been implicated in the generation of protective cell-mediated tumor immunity. We have generated a tumor model in which a well-understood and clearly **immunostimulatory** antigen, influenza hemagglutinin has been transfected into the BALB/c-derived, MHC-class-I-positive, B7-deficient murine mammary carcinoma, MT901. In this model, expression of the influenza hemagglutinin antigen does not alter tumorigenicity in naive but serves as a tumor-rejection target in immunized mice. T-cell-depletion experiments indicate that successful tumor protection can occur following immunization in mice depleted of CD4+ but not CD8+ T cells, suggesting that tumor protection is largely CD8-mediated and CD4-independent. Interestingly, despite the ability of tumor protection to be generated in the absence of CD4+ T cells, effective immunization was clearly dependent on CD40/CD40L as well as CD28/B7 interactions.
IT Miscellaneous Descriptors
tumor immunity; CD28/B7 interactions; CD40/CD40L interactions

L19 ANSWER 2 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:294074 BIOSIS
DN PREV199900294074
TI Protein changes associated with ionizing radiation-induced apoptosis in human prostate **epithelial tumor cells**.
AU Prasad, Sarada C. (1); Soldatenkov, Viatcheslav A.; Kuettel, Michael R.; Thraves, Peter J.; Zou, Xiaojun; Dritschilo, Anatoly
CS (1) Department of Radiation Medicine, Division of Radiation Research, Georgetown University Medical Center, 3970 Reservoir Road NW, TRB-E204A, Washington, DC, 20007-2197 USA
SO Electrophoresis, (April-May, 1999) Vol. 20, No. 4-5, pp. 1065-1074.
ISSN: 0173-0835.
DT Article
LA English
SL English
AB Ionizing radiation (IR) is an important component in the therapy of localized prostate cancer. Identification of protein alterations during IR-induced apoptosis prostate cancer cells is an important step toward understanding the new metabolic status of the dying cell. In the present study, we report changes in protein profile that define the execution phase of the apoptotic response in the in vitro model of tumorigenic radiation-transformed **SV40**-immortalized human prostate epithelial cells (267B1-XR), induced to undergo programmed cell death by IR. We employed an approach that involves use of analytical two-dimensional polyacrylamide gel electrophoresis (2-D PAGE) coupled with Western blotting with specific antisera. Our results point out that apoptotic cells experience significant reduction in the levels of the intermediate filament proteins, keratins-18, 19, vimentin and the associated 14-3-3 adapter proteins. At the same time, molecular chaperones

such as glucose-regulated protein 94, calreticulin, calnexin, and protein disulfide isomerase exhibit marked accumulation in these dying cells. The present data indicate that apoptosis-associated processes in prostate epithelial cells include solubilization of the rigid intermediate filament network by specific proteolysis as well as increased levels of endoplasmic reticulum (ER) proteins with chaperone functions.

IT Methods & Equipment
fluorescence microscopy: confocal laser microscopy: CB, microscopy method; two-dimensional polyacrylamide gel electrophoresis: Analysis/Characterization Techniques: CB, analytical method; Western blot: detection method, detection/labeling techniques

IT Miscellaneous Descriptors
apoptosis; ionizing radiation

L19 ANSWER 3 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:498319 BIOSIS
DN PREV199800498319
TI The C terminus of **E1A** regulates **tumor** progression and **epithelial cell** differentiation.
AU Fischer, Robert S.; Quinlan, Margaret P. (1)
CS (1) Dep. Microbiol. Immmunol., Univ. Tenn., Memphis, TN 38163 USA
SO Virology, (Sept. 30, 1998) Vol. 249, No. 2, pp. 427-439.
ISSN: 0042-6822.
DT Article
LA English
AB The **E1A** gene of adenovirus has been considered both a dominant **oncogene** and a tumor suppressor. It has been reported to induce epithelial cell but to prevent myoblast differentiation. **E1A** enables **oncogenes** that are unable to transform primary cells on their own to do so, yet suppresses tumor progression toward invasion and metastasis. To try to reconcile the seemingly, conflicting **E1A** phenotypes, we examined the expression of epithelial cell specific and characterizing proteins in **immortalized** or tumorigenically transformed primary epithelial cells expressing wild-type **E1A** or a C-terminal mutant that has lost tumor suppressive abilities. All the cell types continued to express cytokeratin. Epithelial cell morphology, social behavior, and growth characteristics were retained by cells expressing wild-type **E1A**, even in the presence of an activated **ras oncogene**. Mutant **E1A**-expressing cells were less well differentiated even in the absence of **ras**. They were specifically defective in cell-cell junctional complexes, such as tight and adherens junctions and desmosomes. There was also a preference for those actin structures prominent in fibroblasts: stress fibers and filopodia, while in the wild-type **E1A** expressing cells, cortical actin and circumferential actin filaments were dominant Thus the **E1A**-mutant-expressing calls were already predisposed to a more advanced tumor stage even when they were only **immortalized** and not transformed. The results suggest the possibility that the C terminus of **E1A** may be involved in regulating epithelial mesenchymal transitions, which have previously been linked to tumor progression.

IT Methods & Equipment
immunofluorescence analysis: analytical method

IT Miscellaneous Descriptors
epithelial cell differentiation; tumor progression regulation

L19 ANSWER 4 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:271635 BIOSIS
DN PREV199800271635
TI Recombinant adeno-associated virus for the generation of autologous, gene-modified tumor vaccines: Evidence for a high transduction efficiency into primary epithelial cancer cells.
AU Maass, Gerhard; Bogedain, Christoph (1); Scheer, Ursula; Michl, Doris; Hoerer, Markus; Braun-Falco, Markus; Volkenandt, Matthias; Schadendorf, Dirk; Wendtner, Clemens M.; Winnacker, Ernst-Ludwig; Kotin, Robert M.; Hallek, Michael
CS (1) MediGene AG, Lochhamer Str. 11, D-82152 Martinsried/Munich Germany
SO Human Gene Therapy, (May 1, 1998) Vol. 9, No. 7, pp. 1049-1059. ISSN: 1043-0342.
DT Article
LA English
AB To explore the potential of recombinant vectors based on recombinant adeno-associated virus (rAAV) for cancer vaccination, we investigated the transduction efficiency of rAAV into cancer cells ex vivo. Infection of human epithelial cancer cell lines with rAAV carrying reporter genes encoding beta-galactosidase (rAAV/LacZ) or luciferase (rAAV/Luc) resulted in high levels of reporter gene expression (>90% positive cells). In marked contrast, rAAV poorly transduced all murine tumor cell lines, as well as human hematopoietic cell lines. Either irradiation or adenovirus infection of tumor cells prior to rAAV infection induced a 10- to 100-fold increase of reporter gene expression. To determine the transduction efficiency of rAAV into primary cancer cells, freshly isolated, irradiated tumor cells from malignant melanoma and ovarian carcinoma patients were infected with rAAV/Luc, resulting in up to 6.9-fold higher levels of gene expression than in a HeLa tumor cell line. Time course experiments with freshly isolated tumor cells infected with rAAV/Luc showed maximal levels of luciferase expression between days 3 and 9 posttransduction. Simultaneous infection of primary tumor cells with up to three rAAV vectors containing genes encoding the **immunostimulatory** proteins B7-2 (CD86), p35 subunit of IL-12, and p40 subunit of IL-12 resulted in high expression of B7-2 in more than 90% of the tumor cells and in the secretion of high levels of IL-12. Taken together, our results demonstrate that rAAV efficiently transduces freshly isolated human, **epithelial tumor cells** and might therefore be a potent tool to produce improved, gene-modified cancer vaccines.
IT Methods & Equipment
gene therapy: therapeutical method; recombinant adeno-associated viral mediated gene transfer: gene transfer method, transduction efficiency
IT Miscellaneous Descriptors
cancer vaccination

L19 ANSWER 5 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:511249 BIOSIS
DN PREV199699233605
TI TGF-beta-1 and Ha-**Ras** collaborate in modulating the phenotypic plasticity and invasiveness of **epithelial tumor cells**.
AU Oft, Martin; Peli, Janos; Rudaz, Claude; Schwarz, Heinz; Beug, Hartmut; Reichmann, Ernst (1)
CS (1) Inst. Suisse Rech. Exp. Cancer, CH-1066 Epalinges Switzerland

SO Genes & Development, (1996) Vol. 10, No. 19, pp. 2462-2477.
ISSN: 0890-9369.
DT Article
LA English
AB Metastasis of **epithelial tumor cells** can be associated with the acquisition of fibroblastoid features and the ability to invade stroma and blood vessels. Using matched in vivo and in vitro culture systems employing fully polarized, mammary epithelial cells, we report here that TGF-beta-1 brings about these changes in **Ras**-transformed cells but not in normal cells. When grown in collagen gels in the absence of TGF-beta, both normal and **Ras**-transformed mammary epithelial cells form organ-like structures in which the cells maintain their epithelial characteristics. Under these conditions, treatment of normal cells with TGF-beta results in growth arrest. The same treatment renders **Ras**-transformed epithelial cells fibroblastoid, invasive, and resistant to growth inhibition by TGF-beta. After this epithelial-fibroblastoid conversion, the **Ras**-transformed cells start to secrete TGF-beta themselves, leading to autocrine maintenance of the invasive phenotype and recruitment of additional cells to become fibroblastoid and invasive. More important, this cooperation of activated Ha-**Ras** with TGF-beta-1 is operative during in vivo tumorigenesis and, as in wound healing processes, is dependent on epithelial-stromal interactions.
IT Miscellaneous Descriptors
AUTOCRINE LOOP; CELL INVASION; **EPITHELIAL TUMOR CELLS**; EPITHELIAL-STROMAL INTERACTIONS; HA-**RAS ONCOGENE**; INVASIVENESS; MOLECULAR GENETICS; PHENOTYPIC PLASTICITY; TGF-BETA; TRANSFORMING GROWTH FACTOR-BETA; TUMOR BIOLOGY; TUMORIGENESIS

L19 ANSWER 6 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:283485 BIOSIS
DN PREV199699005841
TI Detection of genetic alterations in micrometastatic cells in bone marrow of cancer patients by fluorescence in situ hybridization.
AU Muller, Peter (1); Weckermann, Dorothea; Riethmueller, Gert; Schlimok, Guenter
CS (1) Med. Klinik, Zentralklinikum, Stenglinstrasse, 86156 Augsburg Germany
SO Cancer Genetics and Cytogenetics, (1996) Vol. 88, No. 1, pp. 8-16.
ISSN: 0165-4608.
DT Article
LA English
AB Detection of micrometastatic tumor cells in bone marrow of cancer patients has been shown to be of prognostic significance. To further characterize these cells, we combined antibody labeling and fluorescence in situ hybridization (FISH). For detection of numerical changes of chromosome 17, nine patients with proven breast cancer whose bone marrow contained **epithelial tumor cells** were evaluated. **Epithelial cells** were stained by anticytokeratin antibody. Afterwards FISH was performed using an alpha-satellite probe specific for chromosome 17. In a second series hone marrow epithelial cells of eight patients with breast cancer and of six with prostatic cancer were evaluated for the amplification of **HER-2/neu** by using a gene-specific DNA probe. In the first series four

patients had only single epithelial cells in their bone marrow. Only one single cell showed five hybridization signals, whereas all other single cells showed two or less. Five patients had clusters of epithelial cells in bone marrow with or without additional single cells. One hundred four cells had three or more hybridization signals and 103 of these polysomic cells were located in tumor cell clusters. In the second series we could detect **HER-2/neu** amplification in bone marrow **epithelial tumor cells** in two of eight patients with breast cancer but in none of the prostatic cancer patients. These results show that it is possible to detect numerical chromosomal changes and **oncogene** amplification in bone marrow micrometastatic epithelial cells of cancer patients by combining immunophenotyping and FISH.

IT Miscellaneous Descriptors
ANALYTICAL METHOD; BREAST CANCER; CHROMOSOMAL ABERRATION; CHROMOSOME 17; CYTOGENETIC METHOD; **HER-2/NEU** GENE; IMMUNOPHENOTYPING; **ONCOGENE** AMPLIFICATION; PROSTATE CANCER

L19 ANSWER 7 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:270887 BIOSIS
DN PREV199698827016
TI Purification and characterization of a protein that permits early detection of lung cancer: Identification of heterogeneous nuclear ribonucleoprotein-A2/B1 as the antigen for monoclonal antibody 703D4.
AU Zhou, Jun; Mulshine, James L.; Unsworth, Edward J.; Scott, Frank M.; Avis, Ingalill M.; Vos, Michele D.; Treston, Anthony M. (1)
CS (1) Biomarkers Prevention Res. Branch, DCS, NCI 9610 Medical Center Dr., Room 300, Rockville, MD 20850-3300 USA
SO Journal of Biological Chemistry, (1996) Vol. 271, No. 18, pp. 10760-10766.
ISSN: 0021-9258.
DT Article
LA English
AB We have reported that a mouse monoclonal antibody, 703D4, detects lung cancer 2 years earlier than routine chest x-ray or cytomorphology. We purified the 703D4 antigen to elucidate its role in early lung cancer biology, using Western blot detection after SDS-polyacrylamide gel electrophoresis. Purification steps included anion exchange chromatography, preparative isoelectric focusing, polymer-based C-18-like, and analytical C-4 reverse phase high performance liquid chromatography. After 25-50,000-fold purification, the principal immunostaining protein was gt 95% pure by Coomassie staining. The NH-2 terminus was blocked, so CNBr digestion was used to generate internal peptides. Three sequences, including one across a site of alternate exon splicing, all identified a single protein, heterogeneous nuclear ribonucleoprotein-A2 (hnRNP-A2). A minor co-purifying immunoreactive protein resolved at the final C, high performance liquid chromatography step is the splice variant hnRNP-B1. Northern analysis of RNA from primary normal bronchial epithelial cells demonstrated a low level of hnRNP-A2/B1 expression, consistent with immunohistochemical staining of clinical samples, and increased hnRNP-A2/B1 expression was found in lung cancer cells. hnRNP-A2/B1 expression is under proliferation-dependent control in normal bronchial epithelial cell primary cultures, but not in **SV40**-transformed bronchial **epithelial** cells or **tumor cell** lines. With our clinical data, this information suggests that hnRNP-A2/B1

is an early marker of lung epithelial transformation and carcinogenesis.
IT Miscellaneous Descriptors
AMINO-TERMINAL SEQUENCE; ANION-EXCHANGE CHROMATOGRAPHY; DIAGNOSTICS; HTB58 SQUAMOUS CELL; HUMAN NON-SMALL CELL LUNG CANCER NCI-H720 CELL; IB3-1 BRONCHIAL EPITHELIAL CELL; NCI-H157 CELL; NCI-H23 ADENOCARCINOMA CELL; PREPARATIVE ISOELECTRIC FOCUSING; PURIFICATION METHOD; REVERSE PHASE HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

L19 ANSWER 8 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:495747 BIOSIS
DN PREV199598519297
TI Expression of immune regulatory molecules in Epstein-Barr virus-associated
nasopharyngeal carcinomas with prominent lymphoid stroma: Evidence for a functional interaction between **epithelial tumor cells** and infiltrating lymphoid cells.
AU Agathanggelou, Angelo; Niedobitek, Gerald (1); Chen, Renwu; Nicholls, John; Yin, Weibo; Young, Lawrence S.
CS (1) Dep. Pathol., Univ. Birmingham, Birmingham B15 2TT UK
SO American Journal of Pathology, (1995) Vol. 147, No. 4, pp. 1152-1160. ISSN: 0002-9440.
DT Article
LA English
AB Undifferentiated nasopharyngeal carcinomas (UNPC) are characterized by an association with Epstein-Barr virus and an abundant lymphoid stroma. The role of this lymphoid stroma is uncertain but is mostly thought to represent an immune response against viral or tumor antigens. We have analyzed the expression of immune regulatory receptor/ligand pairs in snap-frozen biopsies of 20 UNPCs. All cases were Epstein-Barr virus positive and the virus-encoded latent membrane protein, LMP1, was expressed in 6 cases. By immunohistochemistry, we have demonstrated the expression of CD70 and CD40 in the tumor cells of 16 and 18 cases, respectively. Infiltrating lymphoid cells expressing CD27, the CD70 receptor, and the CD40 ligand were present in all cases. The **Bcl-2** protein was detected in 17 cases. Unexpectedly, tumor cells of 5 cases expressed at least one member of the **B7** family (CD80, CD86, and **B7**-3) and many lymphoid cells expressing the corresponding counter-receptor, CD28, were detected in all cases. Interestingly, 5 of 6 LMP1-positive cases also expressed **B7**, whereas all 14 LMP1-negative cases were also **B7** negative. Our results indicate that T cells and carcinoma cells communicate in the microenvironment of UNPCs and suggest that the presence of a lymphoid stroma may be a requirement for UNPC growth at least in certain stages of tumor development.
IT Miscellaneous Descriptors
IMMUNOHISTOLOGY; IN-SITU HYBRIDIZATION; TUMOR DEVELOPMENT; TUMOR-INFILTRATING CELL PHENOTYPE; UNDIFFERENTIATED NASOPHARYNGEAL CARCINOMA

L19 ANSWER 9 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:316742 BIOSIS
DN PREV199598331042
TI Specific c-myc and max regulation in epithelial cells.
AU Martel, Cecile; Lallemand, Dominique; Cremisi, Chantal (1)
CS (1) INSERM U180, 45 Rue des Saints-Peres, 75270 Paris 006 France
SO Oncogene, (1995) Vol. 10, No. 11, pp. 2195-2205. ISSN: 0950-9232.

DT Article
LA English
AB We have investigated c-myc, max and c-fos mRNA and protein expression in proliferating, quiescent and stimulated immortalized, **SV40** T antigen (LT) transformed and **tumor**-derived **epithelial cells** as well in human primary keratinocytes and have compared them to their expression in fibroblasts. In proliferating immortalized and **tumor**-derived **epithelial cells**, the levels of c-myc, max and c-fos expression were comparable and much higher than in transformed fibroblasts. c-myc and c-fos mRNA and protein levels remained high even during quiescence, when cells stopped dividing. In contrast, whereas max mRNA was constitutively expressed, max protein levels decreased in both fibroblasts and epithelial cells at high cell density. Changing the medium to serum-free medium of confluent epithelial cells induced a complete proliferative response which started with a transient increase in c-fos and c-myc mRNA, followed by the expression of max. Addition of serum to the medium did not induce additional effects. In fibroblasts, similar treatment induced the arrest of c-myc expression and growth, but max expression was also induced in these cells by serum. Our results therefore show that max expression is growth regulated in both immortalized and transformed epithelial as well as fibroblast cells. In contrast, in epithelial cells, c-myc displayed two contrasting behaviors.
IT Miscellaneous Descriptors
A-498 KIDNEY TUMOR; A-549 LUNG CANCER; C-FOS MESSENGER RNA; CARCINOGENESIS; HEP-G-2 HEPATOMA CELLS; HT-29 COLON CANCER; KERATINOCYTES; KIDNEY CELLS; MCF-7 BREAST CANCER; MONKEY CELLS; PROTEIN EXPRESSION; **SV40** T-ANTIGEN

L19 ANSWER 10 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:316622 BIOSIS
DN PREV199598330922
TI A radiation-induced murine ovarian granulosa cell tumor line: Introduction of v-**ras** gene potentiates a high metastatic ability.
AU Yanagihara, Kazuyoshi (1); Nii, Makoto; Tsumuraya, Masaru; Numoto, Michitaka; Seito, Tsutomu; Seyama, Toshio
CS (1) Dep. Mol. Pathol., Res. Inst. Radiat. Biol. Med., Hiroshima Univ., 1-2-3 Kasumi, Minami-ku, Hiroshima 734 Japan
SO Japanese Journal of Cancer Research, (1995) Vol. 86, No. 4, pp. 347-356. ISSN: 0910-5050.
DT Article
LA English
AB A non-metastatic **epithelial tumor cell** line, OV3121, was established from ovarian granulosa cell tumor in B6C3F1 mouse irradiated with 60Co-gamma rays. OV3121 cells showed an epithelial morphology and grew in monolayer with a population doubling time of 28-30 h. The production of estradiol and the expression of cytokeratin confirmed the epithelial origin of the line. No pulmonary metastasis was observed from solid tumors after subcutaneous (s.c.) injection or after intravenous (i.v.) injection of a clonal subline, OV3121-1 cells. We examined the experimental metastasis of individual clones of OV3121-1 cells, containing various introduced viral **oncogenes**: v-Ha-**ras**, v-Ki-

ras, V-fms, v-mos, v-raf, v-src, v-sis, v-fos and v-myc. Among them, only OV3121-1 cells with v-Ha-MuSV or v-Ki-MuSV produced lung colonies at high frequencies. In a more detailed analysis, the v-Ha-**ras** transfectants OV-ras4 and OV-ras7 were found to form colonies in various organs by metastasis from tumors after s.c. injection, as well as lung colonies after i.v. injection. Moderately metastatic OVras7 cells showed high gelatinolytic activity at 72 kDa (MMP-2) and 92 kDa (MMP-9) as compared with the parental OV3121-1 and OV-Neo control cells by zymographic analysis. However, more metastatic OV-ras4 cells produced progressively weaker bands of 72 kDa gelatinolytic activity. No gross alterations in the expression of MMP-1, MMP-3, TIMP-1 and TIMP-2 transcripts were detected in these cell lines. These results suggest that this ovarian granulosa cell tumor line may provide a useful system for understanding the mechanisms by which **oncogenes** influence the occurrence of metastasis.

IT Miscellaneous Descriptors
CARCINOGENESIS; COBALT-60 GAMMA-RAY TREATMENT; KIDNEY METASTASES; LIVER; LUNG; LYMPH NODE; MATRIX METALLOPROTEINASE; MURINE LEUKEMIA VIRUS GENE TRANSFECTION; ONCORNAVIRUS; TISSUE INHIBITOR OF METALLOPROTEINASE TRANSCRIPT EXPRESSION

L19 ANSWER 11 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1994:213229 BIOSIS
DN PREV199497226229
TI Association of HER2/neu expression with sensitivity to tumor-specific CTL in human ovarian cancer.
AU Yoshino, Ichiro; Peoples, George E.; Goedegebuure, Peter S.; Maziarz, Riard; Eberlein, Timothy J.
CS Div. rugical Oncology, Dep. Surgery, Brigham and Women's Hospital, Harvad Med. Sch., 75 Francis St., Boston, MA 02115 USA
SO Journal of Immunology, (1994) Vol. 152, No. 5, pp. 2393-2400.
ISSN: 0022-1767.
DT Article
LA English
AB To study potential sources of tumor-associated Ags in human ovarian cancer, we have established two ovarian tumor cell lines (OvS1 and OvA2) from two ovarian cancer patients, which express the cellular **oncogene** HER2/neu. Corresponding tumor infiltrating lymphocyte cultures have also been established and display an autologous tumor-specific pattern of cytotoxicity that is HLA-A2 restricted. To determine the potential relationship between HER2/neu expression and CTL-mediated cytolysis, we first established tumor cell clones from OvS1. These were categorized as high or low expressors of HER2/neu (cOvS1 + or cOvS1-, respectively, and cOvS1+ clones displayed a significantly higher sensitivity to CTL killing as compared with cOvS1- clones. To modulate the expression of HER2/neu, ovarian cancer cells were treated with **IFN-gamma**. After this exposure, HER2/neu expression was significantly decreased, whereas the expression of HLA Class I was significantly increased. Despite the increase in HLA Class I molecules on the cell surface, CTL-mediated cytolysis of both OvS1 and OvA2 was significantly decreased. **IFN-gamma** treated cOvS1+ clones displayed a similar decrease in sensitivity to CTL killing, whereas **IFN-gamma** treated cOvS1- clones displayed an increase or no change in sensitivity to CTL. To confirm this apparent association

between HER2/neu expression and CTL recognition, melanoma tumor cell lines that were insensitive to ovarian tumor-specific CTL were transfected with the HER2/neu gene. An HLA-A2+ HER2/neu-transfected melanoma cell line was made sensitive to HLA-A2 restricted ovarian tumor-specific CTL but not to HLA-A2 unrestricted CTL, whereas an HLA-A2- HER2/neu-transfected melanoma remained insensitive to HLA-A2 restricted CTL. These results demonstrate that the sensitivity of ovarian **epithelial tumor cells** to CTL-mediated lysis is associated with the level of expression of HER2/neu, suggesting that this **oncogene** product may serve as a source of tumor associated Ags or as an inducer of such peptides. This is the first time in a human tumor system that **oncogene** expression has been related to the induction of antigenicity. These results prompt us to approach new strategies for immunotherapy of cancer.

IT Miscellaneous Descriptors
ANTIGENICITY INDUCTION; CANCER IMMUNOTHERAPY IMPLICATIONS; CYTOTOXIC T-LYMPHOCYTE; HER2/NEU CELLULAR **ONCOGENE**; HLA-A2 BINDING MOTIF; TUMOR-INFILTRATING LYMPHOCYTE

L19 ANSWER 12 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1993:275926 BIOSIS
DN PREV199396006151
TI Human papillomaviruses in premalignant lesions of genital squamous **epithelia** and in **tumour**-derived **cell** lines.
AU Auvinen, Eeva
CS Dep. Virol. and Biochem., Univ. Turku, Turku Finland
SO Annales Universitatis Turkuensis Series A II Biologica-Geographica-Geologica, (1992) Vol. 0, No. 80, pp. 1-47.
ISSN: 0082-6979.
DT Article
LA English
AB In this thesis several aspects of human papillomavirus infections were studied by methods of molecular biology. Different nucleic acid hybridization methods were tested for creating an optimal system for screening clinical specimens for the presence of HPV. Human papillomavirus types 6, 11, 16, 18, 31 and 33 were studied. One question studied was the applicability of genital smear specimens compared to biopsy specimens for the dot blot nucleic acid hybridization test. Smear specimens are easier to take and prepare, and they are more practical in large scale screening tests for the presence of HPV. Smear specimens were found to be positive for **HPV** 6, 11, **16** or 18 with the same frequency as biopsy specimens from the same patients. However, as one of the specimens may give a negative result, testing of both specimens will increase the number of positive diagnoses. Further, different hybridization conditions were tested in the typing of HPV by dot blot hybridization. A high formamide concentration for achieving high stringency, a high SDS concentration for diminishing the background, and the addition of a polymer, such as polyethylene glycol, were found to be optimal for high specificity and relatively high sensitivity of the reaction. These conditions were used for the typing of a large number of HPV specimens. Flatbet scintillation counting was tested in the rapid quantitation of hybridization results. For HPV specimens, nucleic acid is at present the only applicable method for identification of an infection. Scintillation counting thus offers an alternative for quantitative measurement of the hybridization signal. However, there are some problems, such as the

nonspecific binding of radioactive material on the membrane, which cannot be avoided in routine practice, and which will result in false positive interpretations. The gene expression of the main **oncogenic HPV** type, **HPV 16**, was further studied in genital premalignant lesions. Expression of one of the capsid protein, L2, was studied at the mRNA level by in situ hybridization with single-stranded RNA probes. For studying gene expression at the protein level, a fragment from the L2 gene was cloned into a bacterial expression vector and production of the fusion protein was induced. The protein was purified and used for raising antibodies in rabbits. These antibodies were used to study the protein expression in human tissue material by immunohistochemical staining. Expression of the L2 gene was observed in condylomas and in dysplasias in the middle and upper layers of the epithelium. Expression of the E7 gene, an early gene with **oncogenic** potential, was studied at the mRNA level. It was mainly expressed in the middle and upper layers of the dysplastic epithelia. The expression of both genes seemed to be increased with higher grade of dysplasia. To better understand the role of HPV in the development of dysplastic lesions of genital squamous epithelia and in continuous cell growth in vitro, two cell lines were derived from vaginal premalignant lesions. The original lesions were positive for HPV 33 and **HPV 16**, respectively. In the HPV 33 positive cell line, the originally episomal HPV 33 DNA was probably integrated into the cellular DNA during early cell passaging, and was undetectable in the later passages. Either it was present in only a small population of cells, or was absent altogether. Since the cells grow continuously, it is tempting to speculate that HPV has caused the continuous cell growth but is not necessary for the maintenance of **immortalization**. For the **HPV 16** containing cells, an abnormal restriction, and in the cells **HPV 16** has been detected only with PCR. It is possible that **HPV 16** DNA is present in only a small population of cells. In this thesis both the presence of HPV DNA and the expression of mRNA and protein in natural lesions was studied. Since papillomaviruses do not grow in culture, the only material available for HPV studies are natural lesions and cell lines, either derived from natural tissue or constructed by transfection. Further studies on this material may reveal new aspects of papillomavirus infections in humans.

IT Miscellaneous Descriptors
BIOPSY SPECIMENS; CONDYLOMA; DYSPLASIA; E7 GENE EXPRESSION; GENITAL SMEAR SPECIMENS; L2 GENE EXPRESSION; MESSENGER RNA; MOLECULAR DIAGNOSTIC METHOD; PROTEINS; SENSITIVITY; SPECIFICITY; TUMOR; TYPE 11; TYPE 16; TYPE 18; TYPE 31; TYPE 33; TYPE 6

L19 ANSWER 13 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1990:50635 BIOSIS
DN BA89:27999
TI **ONCOGENE** EXPRESSION IN-VIVO BY OVARIAN ADENOCARCINOMAS AND MIXED-MUELLERIAN TUMORS.
AU KACINSKI B M; CARTER D; KOHORN E I; MITTAL K; BLOODGOOD R S; DONAHUE J; KRAMER C A; FISCHER D; EDWARDS R; ET AL
CS DEP. THERAPEUTIC RADIOL., YALE UNIV. SCH. MED., 333 CEDAR ST., NEW HAVEN, CONN. 06510.
SO YALE J BIOL MED, (1989) 62 (4), 379-392.

CODEN: YJBMAU. ISSN: 0044-0086.
FS BA; OLD
LA English
AB Six-micron paraffin sections of paraformaldehyde-fixed specimens of 24 ovarian benign and neoplastic specimens were assayed for tumor cell-specific **oncogene** expression by a sensitive, quantitative in situ hybridization technique with probes for 17 **oncogenes**, beta-actin, and E. coli beta-lactamase. In the benign, borderline, and invasive adenocarcinomas, multiple **oncogenes**, including neu, fes, fms, Ha-**ras**, trk, c-myc, fos, and PDGF-A chains, were expressed at significant levels relative to a housekeeping gene (beta-actin). In the mixed-Mullerian tumors, a rather different pattern of **oncogene** expression was observed, characterized primarily by expression of sis (PDGF-B chain). For the adenocarcinomas, statistical analysis demonstrated that expression of several genes (fms, neu, PDGF-A) was closely linked to others (c-fos, c-myc) known to have important roles in the control of cell proliferation, but only one gene, fms, correlated very strongly with clinicopathologic features (high FIGO histologic grade and high FIGO clinical stage) predictive of aggressive clinical behavior and poor outcome. The authors discuss the role that **tumor epithelial cell** expression of the fms gene product might play in the auto- and paracrine control of growth and dissemination of ovarian adenocarcinomas.
IT Miscellaneous Descriptors
HUMAN NEU FES FMS HA-**RAS** TRK C-MYC FOS **ONCOGENES**
ADENOCARCINOMA

L19 ANSWER 14 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1989:96030 BIOSIS
TI EXPRESSION OF GROWTH FACTORS AND **ONCOGENES** IN NORMAL AND **TUMOR**-DERIVED HUMAN MAMMARY **EPITHELIAL CELLS.**
AU ZAJCHOWSKI D; BAND V; PAUZIE N; TAGER A; STAMPFER M; SAGER R
CS DIV. CANCER GENET., DANA-FARBER CANCER INST., 44 BINNEY ST., BOSTON, MASS. 02115, USA.
SO CANCER RES, (1988) 48 (24 PART 1), 7041-7047.
CODEN: CNREA8. ISSN: 0008-5472.
FS BA; OLD
LA English
AB The expression of genes which may be involved in the regulation of human mammary epithelial cell growth [transforming growth factors .alpha. and .beta.] and tumorigenesis [c-myc, erbB2, epidermal growth factor receptor (EGFR), Ha-**ras**, pS2] has been compared in similarly cultured normal cell strains and tumor cell lines. We have found that the normal breast cells produce high levels of EGFR mRNA, which are translated into nearly 105 low affinity epidermal growth factor-binding molecules/cell. In the estrogen receptor-negative lines examined, the EGFR gene was expressed at levels comparable to those in the normal cells. In contrast, EGFR and transforming growth factor .alpha.mRNAs were reduced in estrogen receptor-positive tumor lines compared to estrogen receptor-negative lines and normal cells. Steady state mRNA levels for transforming growth factor .beta., erbB2, c-myc, and Ha-**ras** in the normal cells were greater than or comparable to those in all of the breast tumor lines.

Furthermore, in the absence of gene amplification, only one of the genes examined (i.e., pS2) was overexpressed in a subset of the tumor cells compared to their normal counterparts. Several reports by other investigators have described overexpression of some of these genes in breast biopsies and in tumor lines in studies lacking normal controls. Thus, our results, in which the same genes were not overexpressed compared to normal cells unless amplified, underscore the importance of including appropriate normal controls in studies aimed at a defining aberrant patterns of gene expression in tumor cells.

IT Miscellaneous Descriptors
MESSENGER RNA TRANSFORMING GROWTH FACTOR EPIDERMAL GROWTH FACTOR TUMORIGENESIS CELL GROWTH GENE EXPRESSION

L19 ANSWER 15 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1987:127668 BIOSIS
DN BA83:66729
TI PARTIAL TRANSFORMATION OF MOUSE FIBROBLASTIC AND EPITHELIAL CELL LINES WITH THE V-MYC **ONCOGENE**.
AU FALCONE G; SUMMERHAYES I C; PATERSON H; MARSHALL C J; HALL A
CS CHESTER BEATTY LAB., INST. CANCER RES., FULHAM ROAD, LONDON SW3 6JB, LONDON.
SO EXP CELL RES, (1987) 168 (1), 273-284.
CODEN: ECREAL. ISSN: 0014-4827.
FS BA; OLD
LA English
AB To investigate the role of the myc gene in mammalian cell transformation, plasmid constructs containing the v-myc **oncogene** and a co-selectable G418 resistance marker were introduced into both mouse fibroblasts (NIH-3T3) and bladder epithelial cells (BBN3 and BBN7). After transfection or microinjection of DNA, no transformed foci could be detected on confluent monolayers but, when the cells were cultured under conditions in which individual cells were allowed to grow and form colonies, morphological transformation was observed. Unlike **ras** -transformed NIH-3T3 cells, v-myc-transformed cells were unable to grow in serum-free medium, and therefore still required exogenous growth factors. v-myc-transformed NIH-3T3 cells were poor at forming foci when co-cultivated with untransformed cells; however, the efficiencies could be increased by addition of EGF to the medium. Both v-myc-transformed fibroblasts and epithelial cells acquired the ability to grow in soft agar, though at efficiencies lower than the corresponding **ras** transformants. Subcutaneous inoculation of v-myc transformed NIH-3T3 cells into nude mice resulted in no tumours within 6 weeks. After protracted periods (2-3 months) a few tumours were detected, but at a frequency barely above that for spontaneous **tumour** formation. **Epithelial cells** transformed by v-myc were either non-tumorigenic or gave a very low incidence of tumours. We conclude that the v-myc **oncogene** induces morphological changes and anchorage independence in immortal mouse fibroblasts and epithelial cell lines but further events are required for the cells to become tumorigenic.

IT Miscellaneous Descriptors
NIH-3T3 MOUSE FIBROBLASTS BBN3 BLADDER EPITHELIAL CELLS BBN7 BLADDER EPITHELIAL CELLS

L19 ANSWER 16 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1986:455389 BIOSIS
DN BA82:112231
TI BINDING AND INTERNALIZATION OF LOW-DENSITY LIPOPROTEIN IN SCC-25 CELLS AND
SV-40 TRANSFORMED KERATINOCYTES A MORPHOLOGIC STUDY.
AU VERMEER B J; WIJSMAN M C; MOMMAAS-KIENHUIS A M; PONEC M
CS UNIV. MED. CENTRE, DEP. DERMATOL., RIJNSBURGERWEG 10, 2333 AA LEIDEN, NETH.
SO J INVEST DERMATOL, (1986) 86 (2), 195-200.
CODEN: JIDEAE. ISSN: 0022-202X.
FS BA; OLD
LA English
AB Binding of low-density lipoproteins (LDL) to the plasma membrane and internalization of low-density lipoprotein receptor complexes were investigated in an **epithelial tumor cell** derived from the tongue (SCC25) and in **SV40**-transformed keratinocytes (SVK14 cells). For light microscopic studies an immunofluorescence technique with antiapoprotein B as well as conjugation procedure by which a fluorochrome 1,1'-dioctadecyl-3,3,3',3'-tetramethyl-indocarbocyanide (DIL) was conjugated with LDL (LDL-DIL) was used. Binding of LDL to the plasma membrane at 4.degree. C was observed in most SCC25 cells but not in SVK14 cells. The internalization of LDL-DIL was absent in SVK14 cells and was excessive in SCC25 cells. In SCC25 cells, internalization of the LDL-DIL particles was heterogeneously distributed over various cells. When a pulse-chase experiment was performed with LDL-DIL, less LDL was internalized into the SCC25 cells in comparison with a continuous label experiment. For the ultrastructural studies LDL conjugated with colloidal gold was used. In the binding experiments at 4.degree. C most LDL-gold particles were attached to the plasma membrane outside coated pigs. During internalization experiments with LDL-gold particles it was observed that within 5-15 min at 37.degree. C several LDL-gold particles were seen in electron-dense structures near the plasma membrane. The electron-dense structures containing LDL-gold, as observed after an internalization period of 5-15 min, may represent the first endosomal compartment as described for transferrin receptors in A431 cells. After a period of 30 min at 37.degree. C the LDL-gold particles were observed in electron-lucent vesicles (multivesicular bodies) and dense bodies. However coated vesicles containing LDL-gold particles were seen sporadically. It is concluded that the route of internalization of LDL into the SCC25 cells differs from that of other cell types. No internalization of LDL gold was found in SVK14 cells, thus, in this respect, the SVK14 cells resemble normal keratinocytes. The morphologic data are in good agreement with biochemical studies published earlier (Ponec M et al, J Invest Dermatol 83:436-440, 1984). Both investigations suggest that LDL receptor activity is modulated during the process of terminal differentiation.
IT Miscellaneous Descriptors
HUMAN CHOLESTEROL 1 1 DIOCTADECYL-3 3 3 3-TETRAMETHYLINDOCARBOCYANIDE

L19 ANSWER 17 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1984:219865 BIOSIS
DN BA77:52849
TI AN INHIBITORY EFFECT OF **TUMOR** PROMOTERS ON HUMAN

EPITHELIAL CELL GROWTH CAN BE DISSOCIATED FROM AN EFFECT ON JUNCTIONAL COMMUNICATION.

AU MCKAY I; COLLINS M; TAYLOR-PAPADIMITRIOU J; ROZENGURT E
CS IMPERIAL CANCER RES. FUND, LONDON WC2A 3PX, UK.

SO EXP CELL RES, (1983) 145 (2), 245-254.
CODEN: ECREAL. ISSN: 0014-4827.
FS BA; OLD
LA English

AB Studies with rodent cells indicated that the abilities of various tumor promoters to inhibit metabolic cooperation correlate with their potencies as mitogens. The effects of the most potent phorbol ester tumor promoter 12-O-tetradecanoyl phorbol-13-acetate (TPA), were examined on metabolic cooperation and growth of human epidermal cells transformed by **SV40** (SVK14 cells). In this system, TPA inhibits junctional communication and at the same concentration also inhibits growth in a reversible fashion. These effects appear to be mediated by binding of phorbol ester to a single class of high affinity binding site with a Kd similar to that reported for rodent cells (Kd = 20.9 nM at 4.degree. C). Further studies on the effects of phorbol esters on other human epithelial cell lines reveal that the inhibitory effects of TPA on growth and metabolic cooperation may be completely dissociated. Alternative mechanisms by which TPA may exert its growth-inhibitory effects are discussed.

IT Miscellaneous Descriptors
HUMAN EPIDERMAL KERATINOCYTE SVK-14 CELL RODENT CELL SV-40 12-O TETRADECANOYL PHORBOL 13 ACETATE METABOLIC COOPERATION INHIBITION

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=> fil medline

FILE 'MEDLINE' ENTERED AT 11:35:15 ON 13 JAN 2000

 FILE LAST UPDATED: 11 JAN 2000 (20000111/UP).  FILE COVERS 1960 TO DATE.

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 COMPLETED.  NOTICE WILL BE GIVEN ONCE THE RELOAD IS COMPLETED AND
 RELOAD DETAILS WILL BE FOUND IN HELP RLOAD.

 OLDMEDLINE,  data from 1960 through 1965 from the Cumulated Index
 Medicus (CIM), has been added to MEDLINE. See HELP CONTENT for details.

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=> d his


     (FILE 'MEDLINE' ENTERED AT 11:08:44 ON 13 JAN 2000)
                DEL HIS Y
L1           765 S EPITHELI? (3A) TUMOR (2W) CELL#
L2         28070 S ONCOGENES+NT/CT
L3            27 S L1 AND L2
L4             3 S L3 AND IMMORTALI?
L5            24 S L3 NOT L4

     FILE 'MEDLINE' ENTERED AT 11:35:15 ON 13 JAN 2000

=> d .med l4 1-3;d .med l5 1-24


L4   ANSWER 1 OF 3  MEDLINE
AN   1999009395     MEDLINE
DN   99009395
TI   The C terminus of E1A regulates tumor progression and
     epithelial cell differentiation [published erratum
     appears in Virology 1998 Dec 5;252(1):285].
AU   Fischer R S; Quinlan M P
CS   Department of Microbiology and Immunology, University of Tennessee,
     Memphis, Tennessee 38163, USA.
SO   VIROLOGY, (1998 Sep 30) 249 (2) 427-39.
     Journal code: XEA. ISSN: 0042-6822.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Cancer Journals; Priority Journals
EM   199901
AB   The E1A gene of adenovirus has been considered both a dominant oncogene
     and a tumor suppressor. It has been reported to induce epithelial cell
but
     to prevent myoblast differentiation. E1A enables oncogenes that are
unable
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to transform primary cells on their own to do so, yet suppresses tumor progression toward invasion and metastasis. To try to reconcile the seemingly, conflicting E1A phenotypes, we examined the expression of epithelial cell specific and characterizing proteins in **immortalized** or tumorigenically transformed primary epithelial cells expressing wild-type E1A or a C-terminal mutant that has lost tumor suppressive abilities. All the cell types continued to express cytokeratin. Epithelial cell morphology, social behavior, and growth characteristics were retained by cells expressing wild-type E1A, even in the presence of an activated ras oncogene. Mutant E1A-expressing cells were less well differentiated even in the absence of ras. They were specifically defective in cell-cell junctional complexes, such as tight and adherens junctions and desmosomes. There was also a preference for those actin structures prominent in fibroblasts: stress fibers and filopodia, while in the wild-type E1A expressing cells, cortical actin and circumferential actin filaments were dominant. Thus the E1A-mutant-expressing cells were already predisposed to a more advanced tumor stage even when they were only **immortalized** and not transformed. The results suggest the possibility that the C terminus of E1A may be involved in regulating epithelial mesenchymal transitions, which have previously been linked to tumor progression. Copyright 1998 Academic Press.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Actins: ME, metabolism
*Adenovirus E1A Proteins: GE, genetics
*Adenovirus E1A Proteins: PH, physiology
*Adenoviruses, Human: GE, genetics
*Adenoviruses, Human: PY, pathogenicity
Cell Differentiation: GE, genetics
Cell Transformation, Neoplastic
Cell Transformation, Viral
Cells, Cultured
Epithelial Cells: CY, cytology
Genes, Suppressor, Tumor
*Genes, Viral
Membrane Proteins: GE, genetics
Membrane Proteins: PH, physiology
Mutation
Oncogenes
Phosphoproteins: GE, genetics
Phosphoproteins: PH, physiology
Rats
Tight Junctions: GE, genetics
Tight Junctions: PH, physiology
Transfection

L4 ANSWER 2 OF 3 MEDLINE
AN 95303482 MEDLINE
DN 95303482
TI Specific c-myc and max regulation in epithelial cells.
AU Martel C; Lallemand D; Cremisi C
CS Unite de Technologie Cellulaire, Institut Pasteur, Paris, France..
SO ONCOGENE, (1995 Jun 1) 10 (11) 2195-205.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199509
AB We have investigated c-myc, max and c-fos mRNA and protein expression in proliferating, quiescent and stimulated **immortalized**, SV40 T antigen (LT) transformed and **tumor**-derived **epithelial cells** as well in human primary keratinocytes and have compared them to their expression in fibroblasts. In proliferating **immortalized** and **tumor**-derived **epithelial cells**, the levels of c-myc, max and c-fos expression were comparable and much higher than in transformed fibroblasts. c-myc and c-fos mRNA and protein levels remained high even during quiescence, when cells stopped dividing. In contrast, whereas max mRNA was constitutively expressed, max protein levels decreased in both fibroblasts and epithelial cells at high cell density. Changing the medium to serum-free medium of confluent epithelial cells induced a complete proliferative response which started with a transient increase in c-fos and c-myc mRNA, followed by the expression of max. Addition of serum to the medium did not induce additional effects. In fibroblasts, similar treatment induced the arrest of c-myc expression and growth, but max expression was also induced in these cells by serum. Our results therefore show that max expression is growth regulated in both **immortalized** and transformed epithelial as well as fibroblast cells. In contrast, in epithelial cells, c-myc displayed two contrasting behaviors.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Cell Division
Cell Line, Transformed
Culture Media, Serum-Free
*DNA-Binding Proteins: GE, genetics
Epithelium: CY, cytology
Epithelium: ME, metabolism
*Gene Expression Regulation
Genes, fos
***Genes, myc**

L4 ANSWER 3 OF 3 MEDLINE
AN 90099299 MEDLINE
DN 90099299
TI Cooperation of c-raf-1 and c-myc protooncogenes in the neoplastic transformation of simian virus 40 large tumor antigen-**immortalized** human bronchial epithelial cells.
AU Pfeifer A M; Mark G E 3d; Malan-Shibley L; Graziano S; Amstad P; Harris C C
CS Laboratory of Human Carcinogenesis, National Cancer Institute, Bethesda, MD 20892.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1989 Dec) 86 (24) 10075-9.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199004

AB Overexpression of c-raf-1 and the myc family of protooncogenes is primarily associated with small cell carcinoma, which accounts for approximately 25% of human lung cancer. To determine the functional significance of the c-raf-1 and/or c-myc gene expression in lung carcinogenesis and to delineate the relationship between protooncogene expression and tumor phenotype, we introduced both protooncogenes, alone or in combination, into human bronchial epithelial cells. Two retroviral recombinants, pZip-raf and pZip-myc, containing the complete coding sequences of the human c-raf-1 and murine c-myc genes, respectively, were constructed and transfected into simian virus 40 large **tumor** antigen-**immortalized** bronchial **epithelial cells** (BEAS-2B); this was followed by selection for G418 resistance. BEAS-2B cells expressing both the transfected c-raf-1 and c-myc sequences formed large cell carcinomas in athymic nude mice with a latency of 4-21 weeks, whereas either pZip-raf- or pZip-myc-transfected cells were nontumorigenic after 12 months. Cell lines established from tumors (designated RMT) revealed the presence of the cotransfected c-raf-1 and c-myc sequences and expressed morphological, chromosomal, and isoenzyme markers, which identified BEAS-2B cells as the progenitor line of the tumors. A significant increase in the mRNA levels of neuron-specific enolase was detected in BEAS-2B cells containing both the c-raf-1 and c-myc genes and derived tumor cell lines. The data demonstrate that the concomitant expression of the c-raf and c-myc protooncogenes causes neoplastic transformation of human bronchial epithelial cells resulting in large cell carcinomas with certain neuroendocrine markers. The presented model system should be useful in studies of molecular events involved in multistage lung carcinogenesis.

CT Check Tags: Animal; Human
*Antigens, Polyomavirus Transforming: GE, genetics
Blotting, Southern
Bronchi
Cell Line
*Cell Transformation, Neoplastic
Chimera
Epithelium
Gene Expression
Immunoassay
Mice
Mice, Nude
Molecular Weight
Neoplasm Transplantation
*Polyomavirus macacae: GE, genetics
Polyomavirus macacae: IM, immunology
*Protein-Tyrosine Kinase: GE, genetics
*Proto-Oncogene Proteins: GE, genetics
Proto-Oncogene Proteins: IP, isolation & purification
***Proto-Oncogenes**
Transfection
Transplantation, Heterologous

L5 ANSWER 1 OF 24 MEDLINE

AN 1999294163 MEDLINE
DN 99294163
TI Bcl-2 inhibits early apoptotic events and reveals post-mitotic multinucleation without affecting cell cycle arrest in human **epithelial tumor cells** exposed to etoposide.
AU Elliott M J; Murphy K M; Stribinskiene L; Ranganathan V; Sturges E; Farnsworth M L; Lock R B
CS The Henry Vogt Cancer Research Institute, J. Graham Brown Cancer Center, Department of Medicine, University of Louisville, KY 40202, USA.
SO CANCER CHEMOTHERAPY AND PHARMACOLOGY, (1999) 44 (1) 1-11. Journal code: C9S. ISSN: 0344-5704.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199908
EW 19990804
AB Defective apoptotic mechanisms are considered to play a role in both the development of malignancy and resistance to chemotherapeutic drugs. The Bcl-2 family of proteins regulate the cellular commitment to survive or die when challenged with various apoptotic stimuli. PURPOSE: The purpose of this study was to identify the point at which Bcl-2 interrupts the apoptotic cascade initiated following exposure of human tumor cells to etoposide. METHODS: A stable Bcl-2-expressing HeLa-transfected clonal cell line, along with its control-vector-transfected counterpart, were utilized in this study. Following etoposide exposure, cells were examined for cell cycle arrest, formation of hyperdiploid cells, apoptotic DNA degradation, loss of plasma membrane integrity, levels of expression of members of the Bcl-2 protein family, caspase activation, degradation of poly(ADP-ribose) polymerase and movement of Bax from cytosol to cellular membrane fractions. RESULTS: Caspase activation, poly(ADP-ribose) polymerase degradation and Bax membrane insertion were initiated rapidly following etoposide removal, concomitantly with cell cycle arrest. Whereas Bcl-2 had no effect on etoposide-induced cell arrest, it interrupted all aspects of apoptosis, including activation of caspases, poly(ADP-ribose) polymerase degradation, DNA fragmentation and loss of plasma membrane integrity. Surprisingly, Bcl-2 also blocked Bax membrane insertion. In addition, Bcl-2 also prevented the increase in cellular levels of Bak, Bax and Bcl-xL, along with degradation of actin and Bax. However, inhibition of etoposide-induced apoptosis by Bcl-2 resulted in the accumulation of giant, multinucleated cells that eventually lost the ability to exclude trypan blue without apoptotic morphology or DNA degradation. CONCLUSIONS: These results indicate that biochemical apoptotic processes are initiated concomitant with etoposide-induced cell cycle arrest and are interrupted by Bcl-2 overexpression. However, the aberrant mitotic events induced by etoposide are sufficient to kill these cells even in the absence of apoptosis.
CT Check Tags: Human; Support, Non-U.S. Gov't
*Antineoplastic Agents, Phytogenic: PD, pharmacology
*Apoptosis: DE, drug effects
Apoptosis: PH, physiology
Caspases: DE, drug effects
Caspases: ME, metabolism
Cell Nucleus: DE, drug effects

Cell Nucleus: UL, ultrastructure
*Cell Transformation, Neoplastic
*Etoposide: PD, pharmacology
Genes, bcl-2: GE, genetics
Hela Cells: DE, drug effects
Mitosis: DE, drug effects
*Proto-Oncogene Proteins c-bcl-2: BI, biosynthesis
Proto-Oncogene Proteins c-bcl-2: PD, pharmacology

L5 ANSWER 2 OF 24 MEDLINE
AN 1998201687 MEDLINE
DN 98201687
TI The ErbB-2/HER2 oncogenic receptor of adenocarcinomas: from orphanhood to multiple stromal ligands.
AU Tzahar E; Yarden Y
CS Department of Biological Regulation, Weizmann Institute of Science, Rehovot, Israel.. liyarden@wiccmail.weizmann.ac.il
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1998 Feb 20) 1377 (1) M25-37. Ref: 120
Journal code: A0W. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Cancer Journals
EM 199806
EW 19980604
AB Extensive clinical and biochemical evidence implicates ErbB-2, a transmembrane tyrosine kinase related to growth factor receptors, in the development, metastasis, and resistance to therapy of multiple, common human carcinomas. Previous attempts to uncover an ErbB-2-specific ligand led to isolation of the neuregulin (NRG) family, but these ligands, like all other growth factors with an EGF-like motif, only indirectly active ErbB-2. On the other hand, biochemical and genetic evidence suggest a non-autonomous function of ErbB-2 in an interactive ErbB signaling network. Accordingly, the oncoprotein acts as a shared signaling subunit of primary growth factor receptors. By stabilizing heterodimers with other ErbB proteins, ErbB-2 prolongs and enhances signal transduction by a large group of stroma-derived growth factors. Furthermore, we have proposed a model in which all ErbB-2 ligands are bivalent and bind to ErbB-2 with low affinity, following high affinity binding to a primary receptor with which ErbB-2 is heterodimerized. Thus the presence of ErbB-2 in relevant ErbB heterodimeric structures on the surfaces of certain **epithelial tumor cells** can amplify signals arising from the binding of stromal ErbB ligands. This effect, in turn, may promote the growth of carcinoma cells.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
*Adenocarcinoma: GE, genetics
Amino Acid Sequence
Breast Neoplasms: GE, genetics
***Genes, erbB-2: GE, genetics**
Ligands

Models, Molecular
Molecular Sequence Data
Prognosis
Sequence Alignment
Signal Transduction

L5 ANSWER 3 OF 24 MEDLINE
AN 97217988 MEDLINE
DN 97217988
TI Detection of MET oncogene/hepatocyte growth factor receptor in lymph node metastases from head and neck squamous cell carcinomas.
AU Galeazzi E; Olivero M; Gervasio F C; De Stefani A; Valente G; Comoglio P M; Di Renzo M F; Cortesina G
CS Department of Clinical Physiopathology, University of Turin School of Medicine, Italy.
SO EUROPEAN ARCHIVES OF OTO-RHINO-LARYNGOLOGY. SUPPLEMENT, (1997) 1 S138-43. Journal code: BK5. ISSN: 0934-2400.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199708
AB The c-MET oncogene encodes the receptor for hepatocyte growth factor/scatter factor (HGF/SF), which is known to stimulate the invasive growth of epithelial cells cultured in vitro. The Met/HGF receptor is a heterodimeric transmembrane tyrosine kinase, which is a prototype for a new family of growth factor receptors. The c-MET oncogene is expressed in several types of epithelial tissue including keratinocytes and is over-expressed in a number of human carcinomas. Studies on various carcinoma cell lines have shown that over-expression and structural alteration of the receptor result in its activation and confer tumorigenesis. We have studied Met/HGF receptor expression in tissue specimens from 34 patients with head and neck squamous cell carcinomas (HNSCC) and in 17 regional lymph node metastases. Western blot analysis was employed, using monoclonal antibodies directed against either the intracellular or extracellular domain of the receptor. Each sample was compared to its normal counterpart. The receptor did not show any major structural alterations in HNSCC tissues, but its expression was increased from 2- to 50-fold in about 70% of tumors. Immunohistochemistry then showed that the same antibodies stained only a few cells in the basal layer of normal squamous **epithelium** but intensely marked **tumor cells**. In the lymph node metastases of Met-positive tumors, receptor expression was maintained and sometimes increased with respect to primary tumors. Immunohistochemical analysis of the metastatic lymph nodes showed that cells were negative in the normal lymphatic tissue and strongly stained in tumor cells. Over-expression of the Met/HGF receptor was found at all tumor stages but was more significant in those associated with enlarged or multiple (N2-N3) lymph node metastases. These data show that expression of the Met/HGF receptor may be involved in the progression of HNSCC towards a metastatic phenotype and may be a useful marker of head and neck tumor cell spread to regional lymph nodes.
CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged

Aged, 80 and over
Antibodies, Monoclonal
Blotting, Western
Carcinoma, Squamous Cell: PA, pathology
*Carcinoma, Squamous Cell: SC, secondary
Cell Division: DE, drug effects
Cells, Cultured
Disease Progression
Dyes: DU, diagnostic use
Epithelium: DE, drug effects
Epithelium: PA, pathology
Gene Expression Regulation, Neoplastic
*Head and Neck Neoplasms: PA, pathology
Hepatocyte Growth Factor: AN, analysis
Hepatocyte Growth Factor: GE, genetics
Hepatocyte Growth Factor: PD, pharmacology
Immunohistochemistry
*Lymphatic Metastasis: PA, pathology
Lymphoid Tissue: PA, pathology
Middle Age
Neoplasm Invasiveness
Oncogenes: GE, genetics
Phenotype
Protein-Tyrosine Kinase: AN, analysis
Protein-Tyrosine Kinase: GE, genetics
*Proto-Oncogene Proteins: AN, analysis
Proto-Oncogene Proteins: GE, genetics
Proto-Oncogene Proteins: PD, pharmacology
*Receptor Protein-Tyrosine Kinase: AN, analysis
Receptor Protein-Tyrosine Kinase: GE, genetics
Receptor Protein-Tyrosine Kinase: PD, pharmacology
Tumor Cells, Cultured
Tumor Markers, Biological: AN, analysis

L5 ANSWER 4 OF 24 MEDLINE
AN 97000055 MEDLINE
DN 97000055
TI TGF-beta1 and Ha-Ras collaborate in modulating the phenotypic plasticity and invasiveness of **epithelial tumor cells**.
AU Oft M; Peli J; Rudaz C; Schwarz H; Beug H; Reichmann E
CS Forschungsinstitut fur Molekulare Pathologie, Wien, Austria.
SO GENES AND DEVELOPMENT, (1996 Oct 1) 10 (19) 2462-77.
Journal code: FN3. ISSN: 0890-9369.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199701
EW 19970104
AB Metastasis of **epithelial tumor cells** can be associated with the acquisition of fibroblastoid features and the ability to invade stroma and blood vessels. Using matched in vivo and in vitro culture systems employing fully polarized, mammary epithelial cells, we report here that TGF-beta1 brings about these changes in Ras-transformed cells but not in normal cells. When grown in collagen gels in the absence of TGF-beta, both normal and Ras-transformed mammary epithelial cells form

organ-like structures in which the cells maintain their epithelial characteristics. Under these conditions, treatment of normal cells with TGF-beta results in growth arrest. The same treatment renders Ras-transformed epithelial cells fibroblastoid, invasive, and resistant to growth inhibition by TGF-beta. After this epithelial-fibroblastoid conversion, the Ras-transformed cells start to secrete TGF-beta themselves, leading to autocrine maintenance of the invasive phenotype and recruitment of additional cells to become fibroblastoid and invasive. More important, this cooperation of activated Ha-Ras with TGF-beta1 is operative during in vivo tumorigenesis and, as in wound healing processes, is dependent on epithelial-stromal interactions.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Cell Line, Transformed
Cell Polarity
*Cell Transformation, Neoplastic
Chick Embryo
Collagen
Epithelium: CY, cytology
Fibroblasts: PA, pathology
Gels
Genes, ras
Growth Substances: PD, pharmacology
Heart
Mammae: CY, cytology
*Mammary Neoplasms, Experimental: PA, pathology
Mice
Mice, Inbred BALB C
Mice, Nude
Neoplasm Invasiveness
*Neoplasms, Glandular and Epithelial: PA, pathology
*Oncogene Protein p21(ras): PH, physiology
Receptors, Transforming Growth Factor beta: AN, analysis
Receptors, Transforming Growth Factor beta: GE, genetics
RNA, Messenger: AN, analysis
Transforming Growth Factor beta: AN, analysis
Transforming Growth Factor beta: GE, genetics
Transforming Growth Factor beta: PD, pharmacology
*Transforming Growth Factor beta: PH, physiology
Tumor Cells, Cultured
Up-Regulation (Physiology)

L5 ANSWER 5 OF 24 MEDLINE
AN 96439101 MEDLINE
DN 96439101
TI c-Myc inactivation by mutant Max alters growth and morphology of NCI-H-630 colon cancer cells.
AU Borr`e A; Cultraro C M; Segal S
CS NCI-Navy Medical Oncology Branch, NIH, Bethesda, Maryland 20889-5105, USA.
SO JOURNAL OF CELLULAR PHYSIOLOGY, (1996 Oct) 169 (1) 200-8.
Journal code: HNB. ISSN: 0021-9541.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199702
EW 19970204
AB The myc gene family has been implicated in multiple cell processes including proliferation, differentiation, tumorigenesis, and apoptosis. For its cellular growth promoting function, Myc must heterodimerize with Max. To study the effect of Myc inactivation on the growth and differentiation properties of **epithelial tumor cells**, we transfected the H-630 human colon cancer cell line with bm-max, a mutant Max protein in which DNA-binding activity has been abolished. Cells expressing high levels of bm-Max grow poorly, and the morphology of both colonies and single cells is altered. Moreover, increased bm-Max expression results in a prolonged G alpha/G1 phase accompanied by induced expression of p21 (WAF1/CIP1), elevated levels of alkaline phosphatase (ALP) activity, and accumulation of large fat granuli within the cells. These distinctive cell characteristics are associated with differentiation processes in numerous malignant cell lines. The results of this study support a model in which sequestering of endogenous Myc and Max proteins into "basic mutant" dimers lacking DNA-binding activity is sufficient both to inhibit proliferation and to induce changes in cell behavior consistent with differentiation.
CT Check Tags: Human; Support, Non-U.S. Gov't
Alkaline Phosphatase: ME, metabolism
Cell Cycle
Cell Division
*Colonic Neoplasms: GE, genetics
Colonic Neoplasms: ME, metabolism
*Colonic Neoplasms: PA, pathology
Cyclins: GE, genetics
*DNA-Binding Proteins: GE, genetics
DNA-Binding Proteins: ME, metabolism
Enzyme Inhibitors
Gene Expression
*Gene Expression Regulation
***Genes, myc**
Lipids: BI, biosynthesis
*Mutation
RNA, Messenger: ME, metabolism
Transfection
Tumor Cells, Cultured

L5 ANSWER 6 OF 24 MEDLINE
AN 95293765 MEDLINE
DN 95293765
TI A radiation-induced murine ovarian granulosa cell tumor line: introduction of v-ras gene potentiates a high metastatic ability.
AU Yanagihara K; Nii M; Tsumuraya M; Numoto M; Seito T; Seyama T
CS Department of Molecular Pathology, Research Institute for Radiation Biology and Medicine, Hiroshima University.
SO JAPANESE JOURNAL OF CANCER RESEARCH, (1995 Apr) 86 (4) 347-56. Journal code: HBA. ISSN: 0910-5050.
CY Japan

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199509
AB A non-metastatic **epithelial tumor cell** line, OV3121, was established from ovarian granulosa cell tumor in B6C3F1 mouse irradiated with 60Co-gamma rays. OV3121 cells showed an epithelial morphology and grew in monolayer with a population doubling time of 28-30 h. The production of estradiol and the expression of cytokeratin confirmed the epithelial origin of the line. No pulmonary metastasis was observed from solid tumors after subcutaneous (s.c.) injection or after intravenous (i.v.) injection of a clonal subline, OV3121-1 cells. We examined the experimental metastasis of individual clones of OV3121-1 cells, containing various introduced viral oncogenes: v-Ha-ras, v-Ki-ras, v-fms, v-mos, v-raf, v-src, v-sis, v-fos and v-myc. Among them, only OV3121-1 cells with v-Ha-MuSV or v-Ki-MuSV produced lung colonies at high frequencies. In a more detailed analysis, the v-Ha-ras transfectants OV-ras4 and OV-ras7 were found to form colonies in various organs by metastasis from tumors after s.c. injection, as well as lung colonies after i.v. injection. Moderately metastatic OV-ras7 cells showed high gelatinolytic activity at 72 kDa (MMP-2) and 92 kDa (MMP-9) as compared with the parental OV3121-1 and OV-Neo control cells by zymographic analysis. However, more metastatic OV-ras4 cells produced progressively weaker bands of 72 kDa gelatinolytic activity. No gross alterations in the expression of MMP-1, MMP-3, TIMP-1 and TIMP-2 transcripts were detected in these cell lines. These results suggest that this ovarian granulosa cell tumor line may provide a useful system for understanding the mechanisms by which oncogenes influence the occurrence of metastasis.
CT Check Tags: Animal; Female
Cell Division: PH, physiology
Cell Division: RE, radiation effects
Cell Transformation, Viral: GE, genetics
Disease Models, Animal
Epithelium: PH, physiology
Epithelium: RE, radiation effects
Gene Expression
*Gene Transfer
***Genes, ras**
Granulosa Cell Tumor: ET, etiology
*Granulosa Cell Tumor: GE, genetics
*Granulosa Cell Tumor: PA, pathology
Liver Neoplasms, Experimental: SC, secondary
Lung Neoplasms: SC, secondary
Mice
Mice, Inbred C3H
Mice, Inbred C57BL
Neoplasm Metastasis
Neoplasm Transplantation
*Neoplasms, Radiation-Induced: GE, genetics
*Neoplasms, Radiation-Induced: PA, pathology
Ovarian Neoplasms: ET, etiology
*Ovarian Neoplasms: GE, genetics

*Ovarian Neoplasms: PA, pathology
Peptide Hydrolases: BI, biosynthesis
Peptide Hydrolases: GE, genetics
Transfection
Transformation, Genetic
Tumor Cells, Cultured
3T3 Cells: PH, physiology

L5 ANSWER 7 OF 24 MEDLINE
AN 94291757 MEDLINE
DN 94291757
TI Paracrine factor and cell-cell contact-mediated induction of protease and c-ets gene expression in malignant keratinocyte/dermal fibroblast cocultures.
AU Borchers A H; Powell M B; Fusenig N E; Bowden G T
CS Department of Radiation Oncology, University of Arizona Medical Center, Tucson 85724.
NC CA-40584 (NCI)
CA-51971 (NCI)
SO EXPERIMENTAL CELL RESEARCH, (1994 Jul) 213 (1) 143-7.
Journal code: EPB. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199410
AB The purpose of this study was to characterize stromal-epithelial interactions that result in induction of protease gene expression in squamous cell carcinoma of the skin. Coculture of the human squamous cell carcinoma cell line II4 with primary human foreskin fibroblasts was observed to induce mRNA expression of urokinase-type plasminogen activator (uPa), matrilysin, 92-kDa type IV collagenase, and c-ets, a transcriptional activator of several genes within the serine and matrix metalloprotease families. uPA and c-ets induction were localized to the fibroblast cell population. uPa induction was found to be dependent upon cell-cell contact with the tumor cell population, whereas c-ets induction was due to a combination of cell-cell contact and a tumor cell-derived soluble factor. In contrast, matrilysin induction localized to the tumor cells and was shown by Northern and Western analyses to occur in response to a fibroblast-derived soluble factor. These data demonstrate that both paracrine factors and cell-cell contact between stromal fibroblasts and **epithelial tumor cells** can influence protease gene expression.
CT Check Tags: Human; Male; Support, U.S. Gov't, P.H.S.
Blotting, Western
*Carcinoma, Squamous Cell: ME, metabolism
*Cell Communication
Cells, Cultured
Collagenases: BI, biosynthesis
Collagenases: IP, isolation & purification
Enzyme Induction
Fibroblasts: ME, metabolism
*Gene Expression Regulation, Neoplastic
*Intercellular Junctions: PH, physiology
*Keratinocytes: ME, metabolism
Metalloproteinases: BI, biosynthesis

Metalloproteinases: IP, isolation & purification
*Peptide Peptidohydrolases: BI, biosynthesis
*Proto-Oncogene Proteins: BI, biosynthesis
***Proto-Oncogenes**
Serine Proteinases: BI, biosynthesis
*Skin: ME, metabolism
*Skin Neoplasms: ME, metabolism
Tumor Cells, Cultured
Urokinase: BI, biosynthesis

L5 ANSWER 8 OF 24 MEDLINE
AN 94179821 MEDLINE
DN 94179821
TI Association of HER2/neu expression with sensitivity to tumor-specific CTL in human ovarian cancer.
AU Yoshino I; Peoples G E; Goedegebuure P S; Maziarz R; Eberlein T J
CS Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115.
NC RO1 CA 45484 (NCI)
CA 09535 (NCI)
SO JOURNAL OF IMMUNOLOGY, (1994 Mar 1) 152 (5) 2393-400.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199406
AB To study potential sources of tumor-associated Ags in human ovarian cancer, we have established two ovarian tumor cell lines (OvS1 and OvA2) from two ovarian cancer patients, which express the cellular oncogene HER2/neu. Corresponding tumor infiltrating lymphocyte cultures have also been established and display an autologous tumor-specific pattern of cytotoxicity that is HLA-A2 restricted. To determine the potential relationship between HER2/neu expression and CTL-mediated cytolysis, we first established tumor cell clones from OvS1. These were categorized as high or low expressors of HER2/neu (cOvS1+ or cOvS1-, respectively), and cOvS1+ clones displayed a significantly higher sensitivity to CTL killing as compared with cOvS1- clones. To modulate the expression of HER2/neu, ovarian cancer cells were treated with IFN-gamma. After this exposure, HER2/neu expression was significantly decreased, whereas the expression of HLA Class I was significantly increased. Despite the increase in HLA Class I molecules on the cell surface, CTL-mediated cytolysis of both OvS1 and OvA2 was significantly decreased. IFN-gamma treated cOvS1+ clones displayed a similar decrease in sensitivity to CTL killing, whereas IFN-gamma treated cOvS1- clones displayed an increase or no change in sensitivity to CTL. To confirm this apparent association between HER2/neu expression and CTL recognition, melanoma tumor cell lines that were insensitive to ovarian tumor-specific CTL were transfected with the HER2/neu gene. An HLA-A2+ HER2/neu-transfected melanoma cell line was made sensitive to HLA-A2 restricted ovarian tumor-specific CTL but not to HLA-A2 unrestricted CTL, whereas an HLA-A2- HER2/neu-transfected melanoma remained insensitive to HLA-A2 restricted CTL. These results demonstrate that the sensitivity of ovarian **epithelial tumor cells** to CTL-mediated lysis is associated with the level of

expression of HER2/neu, suggesting that this oncogene product may serve as a source of tumor-associated Ags or as an inducer of such peptides. This is the first time in a human tumor system that oncogene expression has been related to the induction of antigenicity. These results prompt us to approach new strategies for immunotherapy of cancer.

CT Check Tags: Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antibodies, Monoclonal
Antigens, Neoplasm
Cytotoxicity, Immunologic
HLA-A2 Antigen
Interferon Type II: PD, pharmacology
*Lymphocytes, Tumor-Infiltrating: IM, immunology
Melanoma: GE, genetics
Melanoma: IM, immunology
*Ovarian Neoplasms: GE, genetics
*Ovarian Neoplasms: IM, immunology
***Proto-Oncogenes**
*T-Lymphocytes, Cytotoxic: IM, immunology
Transfection
Tumor Cells, Cultured: IM, immunology

L5 ANSWER 9 OF 24 MEDLINE
AN 94118530 MEDLINE
DN 94118530
TI The Met/hepatocyte growth factor receptor (HGFR) gene is overexpressed in some cases of human leukemia and lymphoma.
AU Jucker M; Gunther A; Gradl G; Fonatsch C; Krueger G; Diehl V; Tesch H
CS Medizinische Klinik I, Universitat Koln, F.R.G.
SO LEUKEMIA RESEARCH, (1994 Jan) 18 (1) 7-16.
Journal code: K9M. ISSN: 0145-2126.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199404
AB The proto-oncogene c-met encodes a heterodimeric (alpha, beta) tyrosine kinase receptor which binds the hepatocyte growth factor (HGF). Recently, overexpression of the Met/HGF receptor gene has been detected in fresh samples of carcinomas and in **epithelial tumor cell** lines but not in cell lines derived from human leukemia and lymphoma. Our analysis of 50 primary samples of human leukemia and lymphoma and 23 hematopoietic cell lines revealed expression of mRNA and protein of the met/HGF receptor in 6 out of the 73 hematopoietic tumor samples analyzed. Four of the six samples positive for expression of the Met/HGF receptor gene were derived from patients with Hodgkin's disease. In addition, in one Burkitt's lymphoma cell line and in one acute myeloid leukemia (AML), expression of the Met/HGF receptor gene was detected. In normal unstimulated lymphocytes, granulocytes or monocytes we did not find expression of the Met/HGF receptor gene. Upon stimulation with the phorbol ester TPA we detected a weak expression of Met/HGF receptor specific transcripts of 9.0 kb in peripheral blood mononuclear cells of a healthy donor. Cytogenetic analyses of three of the four cell lines which express the Met/HGF receptor gene revealed structural or numerical abnormalities

of the long arm of chromosome 7, where the Met/HGFR gene is located, in each of the three cell lines analyzed. In one of these cell lines (L540) the Met/HGFR gene is translocated to a marker chromosome. Southern blot and pulsed field gel electrophoresis experiments did not show any rearrangement in a region of 600 kb around the Met/HGF receptor gene excluding an activation of Met/HGFR by a TPR/Met oncogenic rearrangement as described for MNNG-HOS cells and for some gastric tumors. Our data indicate that the Met/HGFR gene is deregulated in a few cases of human leukemia, Burkitt's lymphoma and Hodgkin's disease possibly by chromosomal rearrangements resulting in an overexpression of the normal Met/HGF receptor mRNA and protein without formation of a hybrid gene.

CT Check Tags: Human; Support, Non-U.S. Gov't
Chromosome Aberrations
Chromosomes, Human, Pair 7
*Gene Expression
Gene Expression Regulation, Leukemic
Gene Expression Regulation, Neoplastic
Hematopoietic Stem Cells: ME, metabolism
Hodgkin Disease: GE, genetics
Hodgkin Disease: ME, metabolism
*Leukemia, Lymphocytic: GE, genetics
Leukemia, Lymphocytic: ME, metabolism
*Leukemia, Myelocytic, Acute: GE, genetics
Leukemia, Myelocytic, Acute: ME, metabolism
*Lymphoma: GE, genetics
Lymphoma: ME, metabolism
Lymphoma, Non-Hodgkin: GE, genetics
Lymphoma, Non-Hodgkin: ME, metabolism
***Proto-Oncogenes: GE, genetics**
*Receptor Protein-Tyrosine Kinase: GE, genetics
Receptor Protein-Tyrosine Kinase: ME, metabolism
RNA, Messenger: ME, metabolism

L5 ANSWER 10 OF 24 MEDLINE
AN 94098333 MEDLINE
DN 94098333
TI The Met proto-oncogene mesenchymal to epithelial cell conversion.
AU Tsarfaty I; Rong S; Resau J H; Rulong S; da Silva P P; Vande Woude G F
CS ABL-Basic Research Program, National Cancer Institute (NCI)-Frederick Cancer Research and Development Center, MD 21702-1201.
NC N01-CO-74101 (NCI)
SO SCIENCE, (1994 Jan 7) 263 (5143) 98-101.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199404
AB Coexpression of the human Met receptor and its ligand, hepatocyte growth factor/scatter factor (HGF/SF), in NIH 3T3 fibroblasts causes the cells to become tumorigenic in nude mice. The resultant tumors display lumen-like morphology, contain carcinoma-like focal areas with intercellular junctions resembling desmosomes, and coexpress epithelial (cytokeratin) and mesenchymal (vimentin) cytoskeletal markers. The tumor cells also display enhanced expression of desmosomal and tight-junction proteins. The

apparent mesenchymal to **epithelial** conversion of the **tumor cells** mimics the conversion that occurs during embryonic kidney development, suggesting that Met-HGF/SF signaling plays a role in this process as well as in tumors that express both epithelial and mesenchymal markers.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
*Cell Transformation, Neoplastic
Desmosomes: UL, ultrastructure
Epithelium: CY, cytology
Hepatocyte Growth Factor: ME, metabolism
Hepatocyte Growth Factor: PD, pharmacology
Keratin: BI, biosynthesis
Kidney: EM, embryology
Kidney: ME, metabolism
Mesoderm: CY, cytology
Mice
Mice, Nude
Neoplasms, Experimental: ME, metabolism
*Neoplasms, Experimental: PA, pathology
Proto-Oncogene Proteins: GE, genetics
*Proto-Oncogene Proteins: ME, metabolism
***Proto-Oncogenes**
Receptor Protein-Tyrosine Kinase: GE, genetics
*Receptor Protein-Tyrosine Kinase: ME, metabolism
Signal Transduction
Transfection
Vimentin: BI, biosynthesis
3T3 Cells

L5 ANSWER 11 OF 24 MEDLINE
AN 94067161 MEDLINE
DN 94067161
TI Glucocorticoids induce a G1/G0 cell cycle arrest of Con8 rat mammary tumor cells that is synchronously reversed by steroid withdrawal or addition of transforming growth factor-alpha.
AU Goya L; Maiyar A C; Ge Y; Firestone G L
CS Department of Molecular and Cell Biology, University of California, Berkeley 94720.
NC CA-05388 (NCI)
CA-09041 (NCI)
SO MOLECULAR ENDOCRINOLOGY, (1993 Sep) 7 (9) 1121-32.
Journal code: NGZ. ISSN: 0888-8809.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199403
AB Con8 mammary **tumor** cells are an **epithelial** **cell** line derived from the 7,12-dimethylbenz(alpha)anthracene-induced 13762NF rat mammary adenocarcinoma. The synthetic glucocorticoid dexamethasone suppresses the growth of Con8 cells, and after 5 days of treatment with this steroid, Con8 cells undergo less than 0.5 population doublings. This growth arrest is accompanied by a 30-fold elevation in c-jun transcript levels, no change in c-fos expression, and a moderate

increase in total AP-1 transcriptional activity. Dexamethasone inhibited DNA synthesis within one cell cycle, and flow cytometry of propidium iodide-stained nuclei demonstrated that dexamethasone growth-suppressed cells had a DNA content indicative of a specific cell cycle block in either G1 or G0. Consistent with a G1/G0 arrest of the cell cycle, dexamethasone did not prevent Con8 cells from entering the S phase after release from synchronization at the G1/S boundary by a double thymidine block. Analysis of [3H]thymidine incorporation and autoradiography of [3H]thymidine-labeled nuclei revealed that after either dexamethasone withdrawal or the addition of transforming growth factor-alpha (TGF alpha), Con8 cells synchronously reinitiate cell cycle progression. Northern blot analysis demonstrated that an induction of transcripts for the G1 marker genes c-myc and cyclin D1 occurs before cells enter the S-phase. After dexamethasone withdrawal, c-myc and cyclin D1 expression transiently peak at 2 and 4 h, respectively. In contrast, c-myc expression peaked at 0.5-1 h, whereas cyclin D1 expression was induced at 2 h and maintained at a high level after the addition of TGF alpha. Our results demonstrate that glucocorticoids induce a specific block of the cell cycle progression of a rat mammary tumor cell, and that after synchronous progression through the cell cycle, the temporal expression pattern for c-myc and cyclin D1 is distinct for dexamethasone release vs. the addition of TGF alpha to glucocorticoid-suppressed cells.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adenocarcinoma
*Cell Cycle: DE, drug effects
Cell Division: DE, drug effects
Chloramphenicol O-Acetyltransferase: BI, biosynthesis
Chloramphenicol O-Acetyltransferase: ME, metabolism
Clone Cells
Cyclins: BI, biosynthesis
*Dexamethasone: PD, pharmacology
DNA, Neoplasm: AN, analysis
*DNA, Neoplasm: BI, biosynthesis
DNA, Neoplasm: DE, drug effects
Gene Expression: DE, drug effects
Genes, myc: DE, drug effects
G0 Phase: DE, drug effects
G1 Phase: DE, drug effects
Kinetics
Mammary Neoplasms, Experimental
Proto-Oncogene Proteins c-myc: BI, biosynthesis
Rats
Thymidine: ME, metabolism
Time Factors
Transcription, Genetic
Transfection
*Transforming Growth Factor alpha: PD, pharmacology
Tumor Cells, Cultured

L5 ANSWER 12 OF 24 MEDLINE
AN 93301781 MEDLINE
DN 93301781
TI Expression of human papillomavirus (HPV) gene in HPV-positive laryngeal

tumors and activity of the HPV long control region in cultured normal laryngeal epithelial cells.
AU Tsutsumi K; Hoshikawa T; Suzuki T; Takeyama I
CS Department of Otorhinolaryngology, St. Marianna University School of Medicine, Kawasaki.
SO NIPPON JIBIINKOKA GAKKAI KAIHO [JOURNAL OF THE OTO-RHINO-LARYNGOLOGICAL SOCIETY OF JAPAN], (1993 May) 96 (5) 767-73.
Journal code: JJZ. ISSN: 0030-6622.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
EM 199309
AB Expression of the human papillomavirus (HPV) gene was examined in HPV-positive laryngeal tumors. Moreover, the activity of the HPV long control region (LCR) was tested in cultured laryngeal epithelial cells. HPV-11 early genes were heterogeneously expressed in adult laryngeal papillomas. We found one laryngeal carcinoma case in whom the HPV-16 transforming genes, E6 and E7, were expressed. Both HPV-11 and -16 LCRs were active in cultured laryngeal epithelial cells from vocal cords. These results suggest that laryngeal **epithelial** and **tumor cells** are target cells for HPV gene expression.
CT Check Tags: Human; Male
Adult
Aged
DNA Probes, HPV
English Abstract
Epithelium: MI, microbiology
Gene Expression Regulation, Viral
Genes, Viral
*Laryngeal Neoplasms: GE, genetics
Laryngeal Neoplasms: MI, microbiology
Larynx: MI, microbiology
Middle Age
Oncogenes
*Papillomavirus: GE, genetics
Transcription, Genetic
Tumor Cells, Cultured

L5 ANSWER 13 OF 24 MEDLINE
AN 93252494 MEDLINE
DN 93252494
TI Establishment and characterization of a human gastric scirrhous carcinoma cell line in serum-free chemically defined medium.
AU Yanagihara K; Kamada N; Tsumuraya M; Amano F
CS Department of Pathology, Hiroshima University, Japan.
SO INTERNATIONAL JOURNAL OF CANCER, (1993 May 8) 54 (2) 200-7.
Journal code: GQU. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199308
AB We have established a human gastric scirrhous carcinoma cell line (designated as HSC-43) in a serum-free chemically defined medium (CDM) without any polypeptide growth factor, from a primary tumor of a 56-year-old male patient. HSC-43 cells grew in vitro in adherence with a

population doubling time of 55 hr, and had the cytological properties of mucinous **epithelial tumor cells**. Cytogenetic analysis of the cells revealed pseudotetraploidy, with structural abnormalities of deletion at chromosome Iq25 and with 3 marker chromosomes. Some cells had retained features of signet-ring cells and caused fibroblastic proliferation when transplanted into athymic nude mice. The possible involvement of transforming growth factor-alpha (TGF-alpha), and its receptor, the epidermal-growth-factor receptor (EGFR), on the growth of HSC-43 cells was studied. Synthesis and secretion of TGF-alpha by HSC-43 cells were confirmed by biological assay and enzyme-linked immunosorbent assay. Radioreceptor analysis showed the presence of receptors for EGF in HSC-43 cells. Proliferation of HSC-43 cells was inhibited by antibodies against TGF-alpha and/or the EGFR. However, neither TGF-alpha nor epidermal growth factor (EGF) was effective in stimulating the cell growth of HSC-43 cells, irrespective of the cell density when supplemented exogenously. Our data suggest that TGF-alpha and EGFR play a role in the autocrine growth of HSC-43 cells. This may be another example of growth regulation of gastric carcinoma.

CT Check Tags: Animal; Human; Male; Support, Non-U.S. Gov't
*Adenocarcinoma, Scirrhous: PA, pathology
Antigens, Tumor-Associated, Carbohydrate: ME, metabolism
Cell Division
Culture Media
DNA, Neoplasm: GE, genetics
Epidermal Growth Factor-Urogastrone: ME, metabolism
Gene Amplification
Karyotyping
Mice
Mice, Nude
Neoplasm Transplantation
Oncogenes
Receptors, Epidermal Growth Factor-Urogastrone: ME, metabolism
*Stomach Neoplasms: PA, pathology
Transforming Growth Factor alpha: ME, metabolism
Transplantation, Heterologous
*Tumor Cells, Cultured

L5 ANSWER 14 OF 24 MEDLINE
AN 93222072 MEDLINE
DN 93222072
TI Glucocorticoids reversibly arrest rat hepatoma cell growth by inducing an early G1 block in cell cycle progression.
AU Sanchez I; Goya L; Vallerga A K; Firestone G L
CS Department of Molecular and Cell Biology, University of California, Berkeley 94720.
NC CA-09041 (NCI)
SO CELL GROWTH AND DIFFERENTIATION, (1993 Mar) 4 (3) 215-25.
Journal code: AYH. ISSN: 1044-9523.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199307
AB We have previously documented that glucocorticoids suppress the

proliferation of BDS1 hepatoma cells, a rat **epithelial tumor cell** line derived from minimal deviation Reuber H35 hepatoma cells. Flow cytometry demonstrated that, after treatment with the synthetic glucocorticoid dexamethasone, the growth of an asynchronous population of BDS1 cells was arrested within one cell cycle which resulted in an accumulation of cells with a G1-G0-like DNA content. Consistent with a glucocorticoid-induced block early in the G1 phase of the cell cycle, propidium iodide flow cytometry revealed that addition of dexamethasone up to 2 h after release from contact inhibition prevented BDS1 hepatoma cells from entering S phase, whereas dexamethasone treatment after 2 h had no effect on the entry of cells into S phase. Moreover, dexamethasone treatment did not prevent BDS1 cells from entering S phase after release from synchronization at the G1-S boundary by a double thymidine block. Analysis of DNA content, [3H]-thymidine incorporation, and autoradiography of [3H]-thymidine-labeled nuclei revealed that, after release from dexamethasone, BDS1 cells synchronously reinitiated cell cycle progression and entered S phase 8 h after hormone withdrawal. Northern blot analysis demonstrated that the level of transcripts encoding the G1 marker genes CYL-1 and CYL-2 G1 cyclins peaked 4 h after dexamethasone withdrawal. Dexamethasone induced a 20-fold increase in the level of c-jun mRNA which was reversed after hormone withdrawal, whereas expression of c-fos transcripts remained at a low level during the time course of hormone treatment and withdrawal. Transient transfections with a collagenase-chloramphenicol acetyltransferase reporter gene showed that dexamethasone inhibited 12-O-tetradecanoylphorbol-13-acetate-inducible, but not basal, AP-1 transcription factor activity. Our results demonstrate that glucocorticoids reversibly induce an early G1 block in cell cycle progression of an **epithelial tumor cell** line that occurs with a coordinate elevation in the expression of c-jun transcripts.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Cell Division: DE, drug effects
*Dexamethasone: PD, pharmacology
*Gene Expression Regulation, Neoplastic: DE, drug effects
***Genes, jun**
*G1 Phase: DE, drug effects
*Liver Neoplasms, Experimental: DT, drug therapy
Liver Neoplasms, Experimental: PA, pathology
Rats
Time Factors
*Transcription, Genetic
Tumor Cells, Cultured

L5 ANSWER 15 OF 24 MEDLINE
AN 92367430 MEDLINE
DN 92367430
TI Oncogene and growth factor expression in ovarian cancer.
AU Kommoss F; Bauknecht T; Birmelin G; Kohler M; Tesch H; Pfleiderer A
CS Department of Gynaecology, Albert-Ludwig University, Freiburg, Germany.

SO ACTA OBSTETRICIA ET GYNECOLOGICA SCANDINAVICA. SUPPLEMENT, (1992) 155 19-24.
Journal code: 1EC. ISSN: 0300-8835.
CY Sweden
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199211
AB The varying tumor-biological behavior of ovarian carcinomas probably influences both their operability and response to chemotherapy, which are the most relevant prognostic factors. The phenotype of different ovarian carcinomas is obviously associated with an activation of the EGF/TGF-alpha signal pathway, including c-myc and c-jun expression. Analysis of EGF-R, TGF-alpha, c-myc and c-jun expression in 33 stage III/IV, and 2 stage I/II ovarian carcinomas with biochemical, molecular-chemical and immunohistochemical methods showed a correlation between the mRNA and protein levels of EGF-R and TGF-alpha for tumors with low or high expressing rates. However, the concentration of measurable free EGF-Rs seems to depend on the amount of TGF-alpha expression by the tumors. The EGF-R binding ligand TGF-alpha is produced by **epithelial tumor cells**; stromal **cells** are usually TGF-alpha-negative, as shown by immunohistochemistry. High expression rates of EGF-R. TGF-alpha and c-myc were detected in 6, 7, and 10 out of 35 ovarian carcinomas, respectively. C-jun mRNA was detected in 18/19 cases studied. Non-malignant tissues originating from myometrium or ovary expressed no (or only small amounts of) EGF-R or TGF-alpha mRNA, whereas a high c-myc expression was found in 1/7 normal myometria, and in 2/5 normal ovaries. There was no strong correlation between EGF-R/TGF-alpha and c-myc/c-jun expression.(ABSTRACT TRUNCATED AT 250 WORDS)
CT Check Tags: Female; Human
Blotting, Northern
*Gene Expression Regulation, Neoplastic
***Genes, jun: GE, genetics**
***Genes, myc: GE, genetics**
Immunohistochemistry
*Ovarian Neoplasms: GE, genetics
*Receptors, Epidermal Growth Factor-Urogastrone: GE, genetics
RNA, Messenger: AN, analysis
Signal Transduction: GE, genetics
*Transforming Growth Factor alpha: GE, genetics

L5 ANSWER 16 OF 24 MEDLINE
AN 91309087 MEDLINE
DN 91309087
TI Isolation of two distinct epithelial cell lines from a single feline mammary carcinoma with different tumorigenic potential in nude mice and expressing different levels of epidermal growth factor receptors.
AU Minke J M; Schuuring E; van den Berghe R; Stolwijk J A; Boonstra J; Cornelisse C; Hilkens J; Misdorp W
CS Department of Veterinary Pathology, State University Utrecht, The Netherlands.
SO CANCER RESEARCH, (1991 Aug 1) 51 (15) 4028-37.
Journal code: CNF. ISSN: 0008-5472.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199110
AB From a single spontaneous feline mammary carcinoma, two subpopulations of **epithelial tumor cells** have been isolated. The variant cells were established as cell lines designated K248C and K248P. DNA ploidy analysis showed that the two cell lines represented cell populations already present in the original tumor. Chromosome analysis confirmed the feline origin of K248C and K248P and demonstrated that in addition to unique marker chromosomes characteristic for each cell line, both cell lines had several marker chromosomes in common. These data suggest that the two cell populations arose from a hypothetical single ancestor which diverged during tumor progression. The K248C and K248P cell lines differed from one another with respect to their tumorigenicity in athymic mice and epidermal growth factor (EGF) receptor content. The K248C cells were highly tumorigenic as indicated by a short latency period and high take rate. The K248P cells were poorly tumorigenic. Southern blot analysis revealed that the K248C cells contained an amplified EGF receptor gene that was accompanied by elevated levels of EGF receptor RNA and protein. The K248C cells were growth inhibited in vitro at EGF concentrations that stimulated growth of K248P cells. The amplification of the EGF receptor gene could be detected only in DNA derived from K248C cells at high passage numbers and not in DNA derived from the original tumor and K248C cells at low passage numbers. These data suggest that amplification of the EGF receptor gene occurred during establishment of the K248C cell line.
CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
Cats
Cell Division: DE, drug effects
DNA: GE, genetics
Epidermal Growth Factor-Urogastrone: ME, metabolism
Epidermal Growth Factor-Urogastrone: PD, pharmacology
Epithelium: PA, pathology
Gene Expression Regulation, Neoplastic: GE, genetics
Karyotyping
Kinetics
Mammary Neoplasms, Experimental: GE, genetics
Mammary Neoplasms, Experimental: ME, metabolism
*Mammary Neoplasms, Experimental: PA, pathology
Mice
Mice, Nude
Neoplasm Transplantation
Oncogenes: GE, genetics
Ploidies
Protein-Tyrosine Kinase: ME, metabolism
*Receptors, Epidermal Growth Factor-Urogastrone: GE, genetics
Receptors, Epidermal Growth Factor-Urogastrone: ME, metabolism
Tumor Cells, Cultured

L5 ANSWER 17 OF 24 MEDLINE
AN 91300540 MEDLINE

DN 91300540
TI Genetic manipulation of E-cadherin expression by **epithelial tumor cells** reveals an invasion suppressor role.
AU Vleminckx K; Vakaet L Jr; Mareel M; Fiers W; van Roy F
CS Laboratory of Molecular Biology, State University of Ghent, Belgium..
SO CELL, (1991 Jul 12) 66 (1) 107-19.
Journal code: CQ4. ISSN: 0092-8674.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199110
AB A cDNA encoding the cell-cell adhesion molecule E-cadherin was transfected into highly invasive **epithelial tumor cell** lines of dog kidney or mouse mammary gland origin. Transfectants with a homogeneously high expression of E-cadherin showed a reproducible loss of activity in two types of in vitro invasion assays. Invasiveness of these transfectants could be reinduced specifically by treatment with anti-E-cadherin antibodies. In vivo, they formed partly differentiated tumors, instead of fully undifferentiated tumors. Alternatively, a plasmid encoding E-cadherin-specific anti-sense RNA was introduced into noninvasive ras-transformed cells with high endogenous E-cadherin expression. The resulting down-regulation, albeit partial, rendered the cells invasive. These data provide direct evidence that E-cadherin acts as an invasion suppressor molecule.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Cadherins: AN, analysis
*Cadherins: GE, genetics
Cell Differentiation
Cell Line
Chick Embryo
Fluorescent Antibody Technique
Genes, ras
Mice
Mice, Nude
Myocardium: PA, pathology
Neoplasm Invasiveness
*Neoplasms, Experimental: GE, genetics
Neoplasms, Experimental: PA, pathology
Plasmids
Transfection

L5 ANSWER 18 OF 24 MEDLINE
AN 91105664 MEDLINE
DN 91105664
TI Establishment and characterization of human signet ring cell gastric carcinoma cell lines with amplification of the c-myc oncogene.
AU Yanagihara K; Seyama T; Tsumuraya M; Kamada N; Yokoro K
CS Department of Pathology, Hiroshima University, Japan.
SO CANCER RESEARCH, (1991 Jan 1) 51 (1) 381-6.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals; Cancer Journals
EM 199105
AB Two unique human signet ring cell gastric carcinoma cell lines (designated HSC-39 and HSC-40A) were established in vitro from the ascites of a 54-year-old male patient. Both cell lines were biologically quite similar, grew in vitro in suspension with a population doubling time of 28-30 h, and had cytological features of mucinous **epithelial tumor cells**. They formed colonies in soft agar, with a cloning efficiency of 0.8-1.0%. Ultrastructurally, numerous granules were observed in the cytoplasm, suggesting secretory activity. The frequent presence of desmosome and the tight junction at the cell boundary certifies the epithelial origin of the lines. Immunocytochemistry and radioimmunoassay showed production of tumor marker antigens (carcinoembryonic antigen, CA 19-9, and sialyl-Lex-i) and gastrin in both lines. These lines were transplantable in athymic BALB/c nude mice. The histopathology of each line growing in athymic BALB/c nude mice was similar to that of the original tumor. The karyotype of the cells was highly aberrant with structural and numerical changes. The presence of numerous double minute chromosomes and loss of the 13 chromosome and Y-chromosome characterize these lines. In addition, the amplified c-myc oncogene (16-32-fold) was found in both cell lines and original ascitic tumor cells. Overexpression of the c-myc mRNA was noted. These cell lines may be a useful tool, providing both in vivo and in vitro systems for further studies of the biology and therapy of human signet ring cell (or Borrmann's type IV carcinoma) gastric carcinoma.
CT Check Tags: Animal; Case Report; Human; Male; Support, Non-U.S. Gov't
Adenocarcinoma, Mucinous: GE, genetics
*Adenocarcinoma, Mucinous: PA, pathology
Blotting, Northern
Blotting, Southern
Gene Amplification
Karyotyping
Mice
Mice, Nude
Microscopy, Electron
Middle Age
Neoplasm Transplantation
*Proto-Oncogene Proteins c-myc: GE, genetics
Proto-Oncogenes
Stomach Neoplasms: GE, genetics
*Stomach Neoplasms: PA, pathology
Tumor Cells, Cultured

L5 ANSWER 19 OF 24 MEDLINE
AN 90085959 MEDLINE
DN 90085959
TI Oncogene expression in vivo by ovarian adenocarcinomas and mixed-mullerian tumors.
AU Kacinski B M; Carter D; Kohorn E I; Mittal K; Bloodgood R S; Donahue J; Kramer C A; Fischer D; Edwards R; Chambers S K; et al
CS Department of Therapeutic Radiology, Yale University School of Medicine, New Haven, CT 06510.
NC CA 47292 (NCI)
SO YALE JOURNAL OF BIOLOGY AND MEDICINE, (1989 Jul-Aug) 62 (4) 379-92.

Journal code: XR7. ISSN: 0044-0086.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199003
AB Six-micron paraffin sections of paraformaldehyde-fixed specimens of 24 ovarian benign and neoplastic specimens were assayed for tumor cell-specific oncogene expression by a sensitive, quantitative in situ hybridization technique with probes for 17 oncogenes, beta-actin, and E. coli beta-lactamase. In the benign, borderline, and invasive adenocarcinomas, multiple oncogenes, including neu, fes, fms, Ha-ras, trk, c-myc, fos, and PDGF-A chains, were expressed at significant levels relative to a housekeeping gene (beta-actin). In the mixed-Mullerian tumors, a rather different pattern of oncogene expression was observed, characterized primarily by expression of sis (PDGF-B chain). For the adenocarcinomas, statistical analysis demonstrated that expression of several genes (fms, neu, PDGF-A) was closely linked to others (c-fos, c-myc) known to have important roles in the control of cell proliferation, but only one gene, fms, correlated very strongly with clinicopathologic features (high FIGO histologic grade and high FIGO clinical stage) predictive of aggressive clinical behavior and poor outcome. The authors discuss the role that **tumor epithelial cell** expression of the fms gene product might play in the auto- and paracrine control of growth and dissemination of ovarian adenocarcinomas.
CT Check Tags: Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Adenocarcinoma: GE, genetics
Adenocarcinoma: PA, pathology
Biopsy
*Gene Expression Regulation, Neoplastic
Neoplasm Staging
*Neoplasms, Germ Cell and Embryonal: GE, genetics
Neoplasms, Germ Cell and Embryonal: PA, pathology
***Oncogenes**
*Ovarian Neoplasms: GE, genetics
Ovarian Neoplasms: PA, pathology
Ovary: PA, pathology
Proto-Oncogene Proteins: GE, genetics

L5 ANSWER 20 OF 24 MEDLINE
AN 89066743 MEDLINE
DN 89066743
TI Glucocorticoids confer normal serum/growth factor-dependent growth regulation to Fu5 rat hepatoma cells in vitro. Sequential expression of cell cycle-regulated genes without changes in intracellular calcium or pH.
AU Cook P W; Weintraub W H; Swanson K T; Machen T E; Firestone G L
CS Department of Physiology-Anatomy, University of California, Berkeley 94720.
NC CA05388 (NCI)
DK19520 (NIDDK)
CA 09041 (NCI)
+
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1988 Dec 25) 263 (36) 19296-302.

Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198903
AB Glucocorticoid hormones induced a stringent dependence on serum for the in vitro proliferation of Fu5 rat hepatoma cells by suppressing the growth rate and final quiescent cell density. Treatment of dexamethasone-suppressed quiescent Fu5 with serum plus insulin caused a rapid reinitiation of cellular proliferation and DNA synthesis that peaked at 16 h. RNA dot blot analysis of this time course showed that the transcript levels for the proto-oncogenes c-fos, c-myc, and c-rasKi peaked at 0.5, 2, and 4 h, respectively, while expression of c-rasHa and ornithine decarboxylase transcripts rose steadily during 16 h. Microspectrofluorimetric measurements of cytosolic calcium (Ca2+i) with fura-2 showed that insulin and serum, alone or in combination, elicited no changes in Ca2+i over a 50-min time course, although ATP, which is not a mitogen, induced large increases in Ca2+i. Cytosolic pH, pHi, was also measured using 2',7'-bis(carboxyethyl)-5(6)-carboxyfluorescein. Insulin and serum, alone or in combination, did not cause pHi to increase in either 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) (pHi 7.17)- or HCO3/CO2 (pHi 7.19)- buffered media. Acid-loading of cells with NH4Cl indicated that both quiescent and proliferating Fu5 cells have equally active, amiloride-sensitive Na/H exchangers. Therefore, induction of DNA synthesis and proto-oncogene expression occurs in Fu5 **epithelial tumor cells** in the absence of any short term increases of pHi or Ca2+i.
CT Check Tags: Animal; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Adenosine Triphosphate: PD, pharmacology
Blood
Calcium: ME, metabolism
Cell Cycle: DE, drug effects
*Cell Division: DE, drug effects
Cell Line
Culture Media
*Dexamethasone: PD, pharmacology
*Estrenes: PD, pharmacology
Gene Expression Regulation: DE, drug effects
***Genes, ras: DE, drug effects**
*Glucocorticoids: AI, antagonists & inhibitors
Kinetics
Liver Neoplasms, Experimental: GE, genetics
*Liver Neoplasms, Experimental: PA, pathology
***Proto-Oncogenes: DE, drug effects**
Rats

L5 ANSWER 21 OF 24 MEDLINE
AN 89051760 MEDLINE
DN 89051760
TI Expression of growth factors and oncogenes in normal and **tumor**-derived human mammary **epithelial cells.**

AU Zajchowski D; Band V; Pauzie N; Tager A; Stampfer M; Sager R
CS Division of Cancer Genetics, Dana-Farber Cancer Institute, Boston, Massachusetts 02115.
NC CA-39814 (NCI)
SO CANCER RESEARCH, (1988 Dec 15) 48 (24 Pt 1) 7041-7.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198903
AB The expression of genes which may be involved in the regulation of human mammary epithelial cell growth [transforming growth factors alpha and beta] and tumorigenesis [c-myc, erbB2, epidermal growth factor receptor (EGFR), Ha-ras, pS2] has been compared in similarly cultured normal cell strains and tumor cell lines. We have found that the normal breast cells produce high levels of EGFR mRNA, which are translated into nearly 10(5) low affinity epidermal growth factor-binding molecules/cell. In the estrogen receptor-negative lines examined, the EGFR gene was expressed at levels comparable to those in the normal cells. In contrast, EGFR and transforming growth factor alpha mRNAs were reduced in estrogen receptor-positive tumor lines compared to estrogen receptor-negative lines and normal cells. Steady state mRNA levels for transforming growth factor beta, erbB2, c-myc, and Ha-ras in the normal cells were greater than or comparable to those in all of the breast tumor lines. Furthermore, in the absence of gene amplification, only one of the genes examined (i.e., pS2) was overexpressed in a subset of the tumor cells compared to their normal counterparts. Several reports by other investigators have described overexpression of some of these genes in breast biopsies and in tumor lines in studies lacking normal controls. Thus, our results, in which the same genes were not overexpressed compared to normal cells unless amplified, underscore the importance of including appropriate normal controls in studies aimed at defining aberrant patterns of gene expression in tumor cells.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
*Breast: ME, metabolism
*Breast Neoplasms: GE, genetics
Breast Neoplasms: ME, metabolism
Cell Line
Epithelium: ME, metabolism
Gene Amplification
Growth Substances: GE, genetics
*Growth Substances: ME, metabolism
***Oncogenes**
Proto-Oncogenes
Receptors, Epidermal Growth Factor-Urogastrone: GE, genetics
Receptors, Estrogen: AN, analysis
RNA, Messenger: ME, metabolism

L5 ANSWER 22 OF 24 MEDLINE
AN 88176895 MEDLINE
DN 88176895
TI Some retinoblastomas, osteosarcomas, and soft tissue sarcomas may share a common etiology.
AU Weichselbaum R R; Beckett M; Diamond A

CS University of Chicago, Department of Radiation and Cellular Oncology, IL 60637..
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1988 Apr) 85 (7) 2106-9.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198807
AB DNA and RNA were extracted from primary human osteosarcomas and soft tissue sarcomas obtained from patients without retinoblastoma and were analyzed by hybridization with a cDNA probe for RB mRNA; absence or alterations of the RB gene are associated with development of retinoblastoma. Most of the osteosarcomas or soft tissue sarcomas examined by us did not express detectable levels of RB mRNA, whereas normal cells and **epithelial tumor cells** did. One osteosarcoma expressed a 2.4-kilobase transcript in addition to a normal 4.7-kilobase species. Our data suggest that transcriptional inactivation or post-transcriptional down-regulation of the RB gene may be important in the etiology of some osteosarcomas and soft tissue sarcomas as well as retinoblastomas.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Bone Neoplasms: GE, genetics
DNA: GE, genetics
DNA, Neoplasm: GE, genetics
*Eye Neoplasms: GE, genetics
Gene Expression Regulation
***Oncogenes**
*Osteosarcoma: GE, genetics
*Retinoblastoma: GE, genetics
RNA, Neoplasm: GE, genetics
*Soft Tissue Neoplasms: GE, genetics

L5 ANSWER 23 OF 24 MEDLINE
AN 88124793 MEDLINE
DN 88124793
TI Characterization of the TPR-MET oncogene p65 and the MET protooncogene p140 protein-tyrosine kinases.
AU Gonzatti-Haces M; Seth A; Park M; Copeland T; Oroszlan S; Vande Woude G F
CS Bionetics Research Inc.--Basic Research Program, National Cancer Institute-Frederick Cancer Research Facility, MD 21701.
NC NO1-CO-23909 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1988 Jan) 85 (1) 21-5.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198805
AB The proteins encoded by the human TPR-MET oncogene (p 65tpr-met) and the human MET protooncogene (p140met) have been identified. The p65tpr-met and

p140met, as well as a truncated TPR-MET product expressed in Escherichia coli, p50met, are autophosphorylated in vitro on tyrosine residues. Using the immunocomplex kinase assay, p140met activity was detected in various human **tumor epithelial cell** lines. In vivo, p65tpr-met is phosphorylated on both serine and tyrosine residues, while p140met is phosphorylated on serine and threonine. p140met is labeled by cell-surface iodination procedures, suggesting that it is a receptor-like transmembrane protein-tyrosine kinase.

CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Cell Line
Cloning, Molecular
Escherichia coli: GE, genetics
Genes, Structural
Molecular Weight
***Oncogenes**
Osteosarcoma
Phosphorylation
*Protein-Tyrosine Kinase: GE, genetics
Protein-Tyrosine Kinase: ME, metabolism
***Proto-Oncogenes**

L5 ANSWER 24 OF 24 MEDLINE
AN 87194480 MEDLINE
DN 87194480
TI Establishment of a rat nasal **epithelial tumor cell** line.
AU Hood A T; Currie D; Garte S J
NC CA36342 (NCI)
ES03563 (NIEHS)
ES00260 (NIEHS)
+
SO IN VITRO CELLULAR AND DEVELOPMENTAL BIOLOGY, (1987 Apr) 23 (4) 274-8.
Journal code: HEQ. ISSN: 0883-8364.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198708
AB A new cell line designated NAS 2BL has been established from a rat nasal tumor induced by inhalation of the direct-acting carcinogen methylmethane sulfonate. The cells are epithelial in morphology, have a generation time of 34 h, require 10% fetal bovine serum for optimal growth, and exhibit keratinization at confluence. The karyotype is aneuploid, with several marker chromosomes, and the cells are transformed by the criterion of nude mouse tumorigenicity.
CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Carcinoma, Squamous Cell: PA, pathology
Cell Division
*Cell Line
Culture Media
Epithelium
Karyotyping
Keratin
*Nasal Mucosa: PA, pathology
*Nose Neoplasms: PA, pathology
Oncogenes

Phenotype
Rats

Inventor Search

Harris 08/981,583

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     (FILE 'BIOSIS' ENTERED AT 11:02:19 ON 13 JAN 2000)
               DEL HIS Y

     FILE 'MEDLINE, BIOSIS, WPIDS, HCAPLUS' ENTERED AT 11:03:17 ON 13 JAN 2000
               E DICKMANNS A/AU
L1           32 S E3-4
               E FANNING E/AU
L2          263 S E3-7 OR E9
               E PANTEL K/AU
L3          286 S E3-4 OR E8
               E RIETHMULLER G/AU
L4          279 S E3-5
L5          805 S L1 OR L2 OR L3 OR L4
L6         6669 S EPITHELI? (3A) (TUMOR OR TUMOUR)
L7           44 S L5 AND L6
L8           43 S L7 AND CELL#
L9           30 DUP REM L7 (14 DUPLICATES REMOVED)

=> d bib ab 1-30


L9   ANSWER 1 OF 30  MEDLINE                                  DUPLICATE 1
AN   1999107231     MEDLINE
DN   99107231
TI   Phenotypic characteristics of cell lines derived from disseminated cancer
     cells in bone marrow of patients with solid epithelial tumors:
     establishment of working models for human micrometastases.
AU   Putz E; Witter K; Offner S; Stosiek P; Zippelius A; Johnson J; Zahn R;
     Riethmuller G; Pantel K
CS   Institute of Immunology, University of Munich, Germany.
SO   CANCER RESEARCH, (1999 Jan 1) 59 (1) 241-8.
     Journal code: CNF. ISSN: 0008-5472.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals; Cancer Journals
EM   199904
EW   19990401
AB   Bone marrow (BM) is a clinically relevant site of micrometastatic disease
     in patients with solid epithelial tumors. It is, therefore, important to
     establish suitable models that allow the in-depth characterization of
     disseminated tumor cells present at low frequencies of 10(-5)-10(-6)
     nucleated BM cells. The aim of this study was to assess common phenotypic
     features of nine tumor cell lines established from BM of patients with
     cancer of the prostate (four cell lines), breast (two cell lines), lung
     (two cell lines), and colon (one cell line) using immunocytochemistry,
     flow cytometry, and reverse transcription-PCR. All cell lines stained
     positive for both cytokeratins, the epithelial intermediate filaments,
and
     the epithelial cell adhesion molecule E-cadherin, and they lacked markers
     of BM-derived cells. The tumor origin of the cell lines was supported by
     the expression of the ErbB2 oncogene (seven of nine) and MAGE mRNA (eight
     of eight). All cell lines coexpressed cytokeratin and vimentin, the
     mesenchymal intermediate filament, indicating an epithelial-mesenchymal
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transition of micrometastatic cells. The invasive phenotype of the immortalized cells was also reflected by the consistent expression of several metastasis-associated adhesion molecules, including alpha5 (eight of nine), alpha6 (five of nine), alphaV (nine of nine), beta1 (nine of nine), and beta3 (nine of nine) integrin subunits and the Mr 67,000 laminin receptor (seven of nine). Contrary to our expectations, metastasis-promoting CD44 variant isoforms were only detected on two lines, whereas all cell lines expressed MUC18/melanoma cell adhesion molecule and intercellular adhesion molecule-1, two members of the immunoglobulin superfamily of adhesion molecules that are not frequently found on primary carcinoma cells. The consistent expression of various **epithelial** and **tumor**-associated antigens provides evidence that the established cell lines are derived from disseminated cancer cells present in the BM. The invasive phenotype of the immortalized cells was mirrored by their epithelial-mesenchymal transition and the expression of several metastasis-associated molecules, which might be potential candidates for novel therapeutic targets.

L9 ANSWER 2 OF 30 MEDLINE DUPLICATE 2
AN 1999456322 MEDLINE
DN 99456322
TI Micrometastatic bone marrow involvement: detection and prognostic significance.
AU Braun S; **Pantel K**
CS Frauenklinik, Klinikum Innenstadt, Ludwig-Maximilians-Universitat, Munchen, Germany.
SO MEDICAL ONCOLOGY, (1999 Sep) 16 (3) 154-65. Ref: 89
Journal code: B3A. ISSN: 1357-0560.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals
EM 200001
EW 20000104
AB The present review focuses on the methodology and clinical significance of new diagnostic approaches to identify individual cancer cells present in bone marrow, both as a frequent site of metastasis formation and an indicator organ for hematogenous tumor cell dissemination. The steadily increasing number of studies on this issue is characterized by considerable methodological variations of important variables, such as the size of the study population, and the reliability of monoclonal antibodies used for tumor cell detection. Emerging data indicate that this disturbing heterogeneity might be overcome by the use of reliable and specific anti-cytokeratin antibodies (for example, A45-B/B3) as, for the time, standard markers for the detection of micrometastatic tumor cells in bone marrow. Prospective clinical studies have shown that immunoassays based on anti-CK antibodies identify patients' subgroups with a poor clinical prognosis with regard to early metastasis manifestation and reduced overall survival in various **epithelial tumor** entities,

including breast, colon, rectum, stomach, esophagus, prostate, renal, bladder, and non-small cell lung cancer. The immunocytochemical assays may be therefore used to improve tumor staging with potential consequences for adjuvant therapy, because disseminated cells appeared to be dormant, non-cycling (for example Ki-67 antigen-negative) cells, suggesting a resistance to cell-cycle dependent therapy, such as chemotherapy. Therefore, cell-cycle independent antibody-based immunotherapy might be an interesting option to complement chemotherapy. Another promising clinical application is monitoring the response of micrometastatic cells to adjuvant therapies, which, at present, can only be assessed retrospectively after an extended period of clinical follow-up. The outlined current strategies for detection and characterization of cancer micrometastasis might help to design and control new therapeutic strategies for secondary prevention of metastatic relapse in patients with operable primary carcinomas.

L9 ANSWER 3 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:297147 BIOSIS
DN PREV199900297147
TI Detection of disseminated **epithelial tumor** cells: Methods and clinical implications.
AU **Pantel, K. (1)**; Witter, K.
CS (1) Institut fuer Immunologie, Ludwig-Maximilians-Universitaet Muenchen, Goethestrasse 31, D-80336, Muenchen Germany
SO Infusionstherapie und Transfusionmedizin, (March, 1999) Vol. 26, No. 2, pp. 96-102.
ISSN: 1019-8466.
DT Article
LA English
SL English; German
AB The most frequent cancers in industrialized societies are derived from epithelia of the gastrointestinal and urogenital tract, as well as of mammary ducts and bronchi. The failure of new early detection methods and improved surgical therapy to decrease the mortality caused by these tumors may be due to the presence of early micrometastatic tumor cell spread, which is usually missed by conventional tumor staging. Analysis of peripheral blood would be obviously the most convenient way to detect hematogeneous tumor cell dissemination. However, the frequency of tumor cells appears to be even lower in blood than in bone marrow. Therefore, we concentrated our work to the detection of bone marrow-derived micrometastatic cancer cells. The biological relevance of circulating tumor cells is unclear since experimental data indicate that most of them do not settle in secondary organs. Nevertheless, tumor cells are more readily found in leukapheresis products used as an increasingly important source of hematopoietic stem cells. Since autologous peripheral stem cell transplantation is a valuable supportive measure which allows the application of high-dose chemotherapy in patients with solid tumors, the detection and elimination of tumor cells in the transplant is of obvious clinical relevance. The present review focuses on diagnostic approaches to identify patients with minimal residual epithelial cancer.

L9 ANSWER 4 OF 30 MEDLINE
AN 1999433366 MEDLINE
DN 99433366
TI Biological characteristics of micrometastatic cancer cells in bone marrow.
AU Braun S; **Pantel K**
CS Frauenklinik, Klinikum Innenstadt, Ludwig-Maximilians-Universitat, Munchen, Germany.
SO CANCER AND METASTASIS REVIEWS, (1999) 18 (1) 75-90. Ref: 131
Journal code: C9H. ISSN: 0891-9992.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200001
EW 20000104
AB There is emerging evidence that **epithelial tumor** cells are able to disseminate to secondary organs at an early stage of primary tumor development. One of the most prominent secondary organs screened for this type of dissemination is bone marrow. Even in cancer entities where overt skeletal metastases are rare (e.g., colorectal and ovarian cancer), bone marrow is a prognostically relevant indicator organ for the presence of hematogenous micrometastases. The currently available data suggest that bone marrow micrometastases represent a selected population of dormant cancer cells which still express a considerable degree of heterogeneity. The analysis of micrometastatic cells will open a new avenue to assess the molecular determinants of early tumor cell dissemination and subsequent outgrowth into overt metastases. Moreover, monitoring the elimination of bone marrow micrometastases and identification of treatment-resistant tumor cell clones may help to increase the efficacy of adjuvant therapy. This review summarizes the current knowledge on the biological characteristics of micrometastatic cancer cells in bone marrow of patients with solid epithelial malignancies.

L9 ANSWER 5 OF 30 MEDLINE DUPLICATE 3
AN 1998422409 MEDLINE
DN 98422409
TI Supersensitive PSA-monitored neoadjuvant hormone treatment of clinically localized prostate cancer: effects on positive margins, **tumor** detection and **epithelial** cells in bone marrow.
AU Kollermann M W; **Pantel K**; Enzmann T; Feek U; Kollermann J; Kossiwakis M; Kaulfuss U; Martell W; Spitz J
CS Department of Urology, Dr. Horst Schmidt Kliniken, Wiesbaden, Germany.
SO EUROPEAN UROLOGY, (1998 Oct) 34 (4) 318-24.
Journal code: ENM. ISSN: 0302-2838.
CY Switzerland
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

EM 199901
EW 19990104
AB OBJECTIVE: The present study was done to investigate the effects of supersensitive PSA-controlled inductive treatment on positive margins, detection of **tumor** and **epithelial** cells in bone marrow of 101 patients with untreated and clinically localized prostatic carcinoma (cT1-3N0M0). METHODS: Hormonal treatment was given until PSA (DPD Immulite(R) third-generation assay) reached <0.1 ng/ml or the nadir value, as shown by two consecutive measurements at monthly intervals. RESULTS: The resultant median duration of treatment was 6 months (range 3-22). Ninety-three (93%) of our patients reached a PSA value <0.1 ng/ml. The nadir of 6 patients (6%) was between 0.1 and 0.3 ng/ml, and it remained >0.3 ng/ml in only 1 case. Of the 101 patients, 82 had a measurable hypoic lesion on initial transrectal ultrasound. 84% of these became smaller, 7.5% remained unchanged and 8.5% increased. Of the 101 prostatectomy specimens, 20 (20%) were margin-positive. The incidence of affected margins was relatively high (35% from 55 patients) with cT3 tumors, but almost negligible (2% from 46 patients) in cT1-2 tumor. Our pathologists, despite their great experience in evaluating hormonally treated prostates (>500 cases) and using immunohistochemical staining, were unable to detect carcinoma in 15 (15%) specimens. Whereas only 2 (4%) of the 55 cT3 specimens were without detectable tumor, this incidence rised to 28% (13 of 46 prostates) in patients with cT1-2 tumors. Of the initial 29 patients with epithelial cells in bone marrow, only 4 (14%) remained positive after controlled induction and all of them had fewer cells than before. CONCLUSION: Endocrine induction controlled by a supersensitive PSA assay and continued until reaching PSA nadir is highly effective in clearing surgical margins and eliminating tumor cells from bone marrow. It seems to be clearly superior to the conventional 3 months of pretreatment at least in cT1-2 tumors in respect to surgical margins and detectability of tumor in the resected prostate. A definitive statement about the value of endocrine induction can only be given by prospective randomized studies, with optimal drugs, doses and treatment time. But the conventional 3 months of pretreatment are far from exploiting the possibilities of this therapeutic option.

L9 ANSWER 6 OF 30 MEDLINE DUPLICATE 4
AN 1999163966 MEDLINE
DN 99163966
TI Prognostic significance of micrometastatic bone marrow involvement.
AU Braun S; **Pantel K**
CS I. Frauenklinik, Klinikum Innenstadt, and Institut fur Immunologie, Ludwig-Maximilians-Universitat, Munchen, Germany.
SO BREAST CANCER RESEARCH AND TREATMENT, (1998) 52 (1-3) 201-16. Ref: 93
Journal code: A8X. ISSN: 0167-6806.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199907
EW 19990701
AB The present review focuses on the methodology and clinical significance of new diagnostic approaches to identify micrometastatic breast cancer cells

present in bone marrow (BM), as a frequent site of overt metastases. Using monoclonal antibodies (mAbs) to **epithelial** cytokeratins (CK) or **tumor**-associated cell membrane glycoproteins, individual carcinoma cells can be detected on cytologic BM preparations at frequencies of 10(-5) to 10(-6). Prospective clinical studies have shown that the presence of these immunostained cells is prognostically relevant with regard to relapse-free and overall survival. The current interest in autologous bone marrow transplantation in patients with solid tumors further underlines the need for screening methods that allow the detection of minute numbers of residual tumor cells in the transplant. Although the development of new molecular detection methods based on the amplification of a marker mRNA species by the polymerase chain reaction technique is a very exciting area of research, the clinical significance of this approach needs to be demonstrated in prospective studies. The immunocytochemical assays may be, therefore, used to improve tumor staging with potential consequences for adjuvant therapy. Another promising clinical application is monitoring the response of micrometastatic cells to adjuvant therapies, which, at present, can only be assessed retrospectively after an extended period of clinical follow-up. The extremely low frequency of BM tumor cells greatly hampers approaches to obtain more specific information on their biological properties. The available data indicate that these cells represent a selected population of cancer cells which, however, still express a considerable degree of heterogeneity with regard to the expression of MHC class I antigens, adhesion molecules (EpCAM), growth factor receptors (EGF receptor, erb-B2, transferrin receptor), or proliferation-associated markers (Ki-67, p120). Regardless of the detection technique applied, there is an urgent demand for large multicentre trials, in which standardized methods are related to specified clinical outcomes.

L9 ANSWER 7 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:143747 BIOSIS
DN PREV199900143747
TI Detection and characterization of minimal residual cancer in patients with epithelial solid tumors.
AU **Pantel, Klaus (1)**
CS (1) Inst. Immunologie, Ludwig-Maximilians-Univ. Muenchen, Goethestr. 31, 80336 Muenchen Germany
SO Bone Marrow Transplantation, (Nov., 1998) Vol. 22, No. SUPPL. 3, pp. S30-S33.
Meeting Info.: 4th International Symposium on High-dose Chemotherapy and Stem Cell Transplantation in Solid Tumors Berlin, Germany April 18-19, 1998
ISSN: 0268-3369.
DT Conference
LA English

L9 ANSWER 8 OF 30 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
DUPLICATE 5
AN 1997-087373 [08] WPIDS

DNN N1997-071901 DNC C1997-028474
TI New immortalised **epithelial tumour** cells - having immortalising oncogene introduced into genome(s) or another replicating genetic element.
DC B04 D16 S03
IN **DICKMANNS, A; FANNING, E; PANTEL, K; RIETHMULLER, G;** RIETHMUELLER, G
PA (MICR-N) MICROMET GMBH
CYC 72
PI WO 9700946 A1 19970109 (199708)* EN 47p
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AU AZ BB BG BR BY CA CN CZ EE GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LV MD MG MK MN MW MX NO NZ PL RO RU SD SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9664153 A 19970122 (199719)
NO 9706036 A 19980203 (199816)
EP 839183 A1 19980506 (199822) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 11507834 W 19990713 (199938) 44p
ADT WO 9700946 A1 WO 1996-EP2747 19960624; AU 9664153 A AU 1996-64153 19960624; NO 9706036 A WO 1996-EP2747 19960624, NO 1997-6036 19971222; EP 839183 A1 EP 1996-923904 19960624, WO 1996-EP2747 19960624; JP 11507834 W WO 1996-EP2747 19960624, JP 1997-503590 19960624
FDT AU 9664153 A Based on WO 9700946; EP 839183 A1 Based on WO 9700946; JP 11507834 W Based on WO 9700946
PRAI EP 1995-109860 19950623
AB WO 9700946 A UPAB: 19970220
Epithelial tumour cell (ETC) with metastatic potential comprises integrated in its genome or another replicative genetic element an externally introduced immortalising oncogene which is expressed in the cell.

Also claimed is an antibody or fragment or deriv. of the antibody or fragment which specifically recognises a tumour cell such as ETC.

USE - The ETC or antibody can be used for the prophylaxis and/or treatment of cancer and/or cancer metastasis. They can also be used for the prepn. of tumour vaccines. They can also be used in diagnostic compsns. The ETC can also be used for the ex vivo stimulation of a patient's immune cells. The cells are used in pharmaceutical and diagnostic compsn. (all claimed).

ADVANTAGE - The ETCs provide for the specific and unlimited expansion of **tumour** cells of **epithelial** origin with metastatic potential.

Dwg.0/5

L9 ANSWER 9 OF 30 MEDLINE DUPLICATE 6
AN 97358747 MEDLINE
DN 97358747
TI Limitations of reverse-transcriptase polymerase chain reaction analyses for detection of micrometastatic epithelial cancer cells in bone marrow [see comments].
CM Comment in: J Clin Oncol 1998 Feb;16(2):806-7
AU Zippelius A; Kufer P; Honold G; Kollermann M W; Oberneder R; Schlimok G; **Riethmuller G; Pantel K**
CS Institut fur Immunologie der Universitat Munchen, Germany.
SO JOURNAL OF CLINICAL ONCOLOGY, (1997 Jul) 15 (7) 2701-8.

Journal code: JCO. ISSN: 0732-183X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Cancer Journals; Priority Journals
EM 199710
AB PURPOSE: This study was designed to evaluate the potential of reverse-transcriptase polymerase chain reaction (RT-PCR) analyses for the detection of micrometastatic carcinoma cells in bone marrow (BM). PATIENTS AND METHODS: The specificity of RT-PCR assays with primers specific for various tumor-associated and organ-specific mRNA species was examined by analysis of 53 BM aspirates from control patients with no epithelial malignancy. In addition, BM samples from 63 patients with prostate cancer (n = 53) or breast cancer (n = 10) were analyzed by RT-PCR with primers specific for prostate-specific antigen (PSA) mRNA. As a reference method, all samples were analyzed simultaneously by an established immunocytochemical assay, using monoclonal antibodies (mAbs) against cytokeratins (CK) for tumor-cell detection. RESULTS: Seven of eight marker species could be detected in a considerable number of BM samples from control patients: epithelial glycoprotein-40 (EGP-40; 53 of 53 samples), desmoplakin I (DPI I; five of five), carcinoembryonic antigen (CEA; five of 19), erb-B2 (five of seven), erb-B3 (six of seven), prostate-specific membrane antigen (PSM; four of nine), and CK18 (five of seven). Only PSA mRNA was not detected in any of the 53 control BM samples. In serial dilution experiments, the PSA RT-PCR assay was able to detect five LNCaP prostate carcinoma cells in 4 x 10(6) BM cells. CK-positive cells were found in 20 patients (37.7%) with prostate cancer, while PSA mRNA was found in only 15 (28.3%; P = .04). Moreover, despite the recent observation that PSA is also expressed in mammary carcinomas, none of the 10 CK-positive BM samples were PSA mRNA-positive. CONCLUSION: Limiting factors in the detection of micrometastatic tumor cells by RT-PCR are (1) the illegitimate transcription of **tumor**-associated or **epithelial**-specific genes in hematopoietic cells, and (2) the deficient expression of the marker gene in micrometastatic tumor cells.

L9 ANSWER 10 OF 30 MEDLINE DUPLICATE 7
AN 97185964 MEDLINE
DN 97185964
TI Occult **epithelial tumor** cells detected in bone marrow by an enzyme immunoassay specific for cytokeratin 19.
AU Hochtlen-Vollmar W; Gruber R; Bodenmuller H; Felber E; Lindemann F; Passlick B; Schlimok G; **Pantel K; Riethmuller G**
CS Institute of Immunology, University of Munich, Germany.
SO INTERNATIONAL JOURNAL OF CANCER, (1997 Feb 7) 70 (4) 396-400. Journal code: GQU. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199705
EW 19970502
AB The presence of isolated carcinoma cells detected immunocytochemically in bone marrow has been shown to be of prognostic relevance for cancer patients. Unfortunately, the immunocytochemical method (ICC) is laborious and depends on the subjective interpretation of the individual

investigator. Therefore, an immunoassay was designed for detection of cytokeratin 19 (CK19). By analyzing blood samples from 52 healthy volunteers and 40 bone-marrow aspirates from control patients, a cut-off point of 250 pg/ml CK19 was determined. Application of this cut-off point enabled a specificity of 95% to be shown for bone marrow and of nearly 100% for venous blood. The assay detected 10 HT-29 colon-carcinoma cells among 5 x 10(6) peripheral-blood leukocytes. In comparison with controls, bone-marrow samples of cancer patients were found to have significantly elevated levels of CK19 ($p < 0.05$). In the analysis of 386 marrow aspirates of cancer patients, a significant concordance of ELISA and ICC was observed (chi 2 = 18.3; $p < 0.001$). Both procedures, nevertheless, differed in 147 (38%) samples, of which more than two thirds (101) were only ELISA-positive. The CK status detected by ELISA did not correlate with the TNM stage and the histological grading. The established immunoassay allowed sensitive and specific detection of disseminated **epithelial tumor** cells and appeared to be faster, less laborious and more objective than ICC. Follow-up studies are required to assess the prognostic relevance of this ELISA before it can be applied as a routine method for monitoring of minimal residual epithelial cancer.

L9 ANSWER 11 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:390638 BIOSIS
DN PREV199699112994
TI Progress in Histochemistry and Cytochemistry, Vol. 30. No. 3. Minimal residual epithelial cancer: Diagnostic approaches and prognostic relevance.
AU **Pantel, K. (1)**; Braun, S.; Passlick, B.; Schlimok, G.
CS (1) Inst. Immunologie, Ludwig-Maximilians-Univ., Goetherstrasse 31, D-80336 Muenchen Germany
SO **Pantel, K.**; Braun, S.; Passlick, B.; Schlimok, G.. Progress in Histochemistry and Cytochemistry, (1996) Vol. 30, No. 3, pp. vii+62p. Progress in Histochemistry and Cytochemistry; Minimal residual epithelial cancer: Diagnostic approaches and prognostic relevance. Publisher: Gustav Fischer Verlag Villengang 2, Jena, Germany. ISSN: 0079-6336. ISBN: 3-437-11712-2, 1-56081-438-1.
DT Book
LA English
AB This text is a review of immunocytochemical approaches to detect and characterize isolated **epithelial tumor** cells present in secondary mesenchymal organs. Seven sections comprise the text. Topics discussed include methodological studies on the immunocytochemical detection of isolated residual tumor cells in mesenchymal organs, prognostic relevance of individual disseminated tumor cells, and immunocytochemical monitoring of therapeutic effects. Immunocytochemical phenotyping of individual disseminated carcinoma cells and the development of new diagnostic techniques are also examined. Diagrams, tables, graphs, and color micrographs are incorporated into the text. References are provided at the end of the text.

L9 ANSWER 12 OF 30 MEDLINE DUPLICATE 8
AN 96374341 MEDLINE
DN 96374341
TI Immunocytochemical detection of disseminated tumor cells in the bone marrow of patients with esophageal carcinoma.
AU Thorban S; Roder J D; Nekarda H; Funk A; Siewert J R; **Pantel K**
CS Department of Surgery, Technische Universitat Munchen, Federal Republic of

Germany.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1996 Sep 4) 88 (17) 1222-7.
Journal code: J9J. ISSN: 0027-8874.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199612
AB BACKGROUND: Approximately half of the patients diagnosed with localized esophageal cancer die of metastatic disease within the first 2 years following tumor resection. The development of monoclonal antibodies (MAbs) directed against **epithelial** cell-associated and **tumor** antigens has enabled the detection of single disseminated tumor cells in secondary organs. PURPOSE: We used MAbs directed against epithelial cell antigens (i.e., cytokeratins) to determine the proportion of patients with esophageal cancer who display isolated tumor cells in their bone marrow. In addition, we evaluated the prognostic significance of a finding of bone marrow tumor cells in patients with esophageal cancer whose tumors were completely resected. METHODS: Prior to the initiation of treatment, bone marrow was aspirated from both sides of the upper iliac crests of 90 patients with squamous cell carcinoma of the esophagus. Bone marrow was also obtained from a population of 30 individuals who had not been diagnosed with cancer. Tumor cells in cytologic bone marrow preparations were detected by use of an assay that employed the MAbs CK2 (directed against cytokeratin 18), KL1 (directed against a 56,000-kd pan-cytokeratin component), and A45-B/B3 (directed against an epitope common to cytokeratins 8, 18, and 19) plus the alkaline phosphatase anti-alkaline phosphatasestaining method. Bone marrow biopsies, for conventional histologic examination with Giemsa staining, were performed on 62 patients. The Kaplan-Meier method and the logrank test were used to assess disease-free and overall survival according to the presence or absence of tumor cells in the bone marrow of 42 patients with completely resected tumors. Reported P values are two-sided. RESULTS: Cytokeratin-positive tumor cells were detected in the bone marrow of 37 (41.1%) of the 90 total patients. The number of tumor cells detected per 10(5) mononuclear bone marrow cells ranged from one to 82. No significant differences in the numbers of disseminated tumor cells were noted for patients diagnosed with tumors at different stages. Only two (3.2%) of 62 bone marrow specimens examined after Giemsa staining showed morphologically identifiable tumor cells. Tumor cells were not detected in the bone marrow of patients who had not been diagnosed with cancer. After a median follow-up of 15.5 months (range, 6-33 months), 15 (79.0%) of 19 patients with completely resected tumors and tumor cells in their bone marrow had relapses compared with three (13.0%) of 23 patients with completely resected tumors and no tumor cells in their bone marrow (P = .019, logrank test). Patients with completely resected tumors and tumor cells in their bone marrow had significantly shorter overall survival than corresponding patients without tumor cells in their bone marrow (P = .036, logrank test). CONCLUSIONS AND

IMPLICATIONS: Dissemination of esophageal cancer cells to the bone marrow is more frequent than expected from the rare occurrence of overt skeletal metastases. In general, the presence of tumor cells in the bone marrow may be an indicator of the disseminatory potential of individual tumors.

L9 ANSWER 13 OF 30 MEDLINE
AN 97214239 MEDLINE
DN 97214239
TI [Expression of plakoglobin in bronchial carcinomas: incidence and significance for disease outcome].
Expression von Plakoglobin bei Bronchialkarzinomen: Haufigkeit und Bedeutung fur den Krankheitsverlauf.
AU Passlick B; **Pantel K**; Stosiek P; Hosch S; Thetter O; Izbicki J R
CS Chirurgische Klinik, Klinikum Innenstadt, Ludwig-Maximilians-Universitat Munchen.
SO LANGENBECKS ARCHIV FUR CHIRURGIE. SUPPLEMENT. KONGRESSBAND, (1996) 113 810-3.
Journal code: BAD. ISSN: 0942-2854.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 199706
EW 19970603
AB Loss of homotypic cell adhesion is an important prerequisite for invasion and metastasis of **epithelial tumor** cells. The function of E-cadherin, which mediates epithelial cell-cell adhesion, is regulated by a complex of proteins bound to its cytoplasmic tail, including a-, b-, g-catenins and plakoglobin (PG). The present study was designed to assess whether downregulation of plakoglobin expression occurs in human non-small cell lung carcinomas (NSCLC) and whether this change is associated with an unfavorable prognosis. Using immunohistochemistry with monoclonal antibody (mAb) PG 5.1 to PG, absence or severely reduced expression of PG (i.e., less than 30% of positive tumor cells) was observed in 39 of 97 patients (40.2%) with completely resected primary NSCLC (stages T1-3, N1-2, M0). There was no significant correlation to any of the analyzed clinicopathologic factors such as histologic type, grade or size of the primary tumor, and lymph node involvement. After a median observation period of 39 months (12-56 mo.), univariate Kaplan-Meier analysis showed that patients with PG-deficient primaries tended to have a shortened disease-free survival (p = 0.06). This correlation was statistically significant in patients with adenocarcinomas (p = 0.010), locally restricted primary tumors (pT1/2, p = 0.017), and negative lymph nodes (pN0, p = 0.036). Analysis of the overall survival in these subgroups also revealed significant associations between deficient PG expression and poor outcome (p < or = 0.036). Multivariate analysis was performed for the largest subgroup of patients with pT1/2 tumors (n = 66), demonstrating that PG expression was a strong, independent predictor of tumor relapse (p = 0.002). Thus, deficient expression of PG is a frequent, early event in the progression of NSCLC, which appears to predict an unfavorable

prognosis in patients at earlier stages of their disease.

L9 ANSWER 14 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:158624 BIOSIS
DN PREV199698730759
TI Frequency and prognostic significance of isolated tumour cells in bone marrow of patients with non-small-cell lung cancer without overt metastases.
AU **Pantel, Klaus (1)**; Izbicki, Jakob; Passlick, Bernward; Angstwurm, Matthias; Haeussinger, Karl; Thetter, Olaf; Riethmueller, Gert
CS (1) Inst. Immunol., Ludwig-Maximillians-Univ., 80336 Muenchen Germany
SO Lancet (North American Edition), (1996) Vol. 347, No. 9002, pp. 649-653. ISSN: 0099-5355.
DT Article
LA English
AB Background: Metastasis is generally looked on as a late event in the natural history of epithelial tumours. However, the poor prognosis of patients with apparently localised lung cancer indicates that micrometastases occur often before diagnosis of the primary tumour. Methods: At primary surgery, disseminated tumour cells were detected immunocytochemically in bone marrow of 139 patients with non-small-cell lung carcinomas without evidence of distant metastases (pT-1-4pN-1-2M-0). Tumour cells in bone-marrow aspirates were detected with monoclonal antibody CK2 against cytokeratin polypeptide 18. Patients were followed up for a median of 39 months (range 14-52) after surgery. 215 patients without epithelial cancer (i.e., with benign epithelial tumours, nonepithelial neoplasms, or inflammatory diseases) acted as controls. Findings: In 83 of 139 (59.7%) patients cytokeratin-positive cells were detected at frequencies of 1 in 100000 to 1 in 1000000. Even without histopathological involvement of lymph nodes (pN-0), tumour cells were found in 38 of 70 (54.3%) patients. 1 positive cell was found in each of 6 out of 215 controls. Surgical manipulation during primary tumour resection did not affect the frequency of these cells. In Cox's regression analyses, the presence of such cells was a significant and independent predictor for a later clinical relapse in node-negative patients (p=0.028). Interpretation: Early dissemination of isolated tumour cells is a frequent and intrinsic characteristic of non-small-cell lung carcinomas. The finding of these cells may help to decide whether adjuvant systemic therapy is required for the individual patient.

L9 ANSWER 15 OF 30 MEDLINE
AN 96268101 MEDLINE
DN 96268101
TI Disseminated **epithelial tumor** cells in bone marrow of patients with esophageal cancer: detection and prognostic significance.
AU Thorban S; Roder J D; Nekarda H; Funk A; **Pantel K**; Siewert J R
CS Department of Surgery, Technical University of Munich, Germany.
SO WORLD JOURNAL OF SURGERY, (1996 Jun) 20 (5) 567-72; discussion 572-3. Journal code: XO8. ISSN: 0364-2313.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

LA English
EM 199610
AB Minimal residual disease in patients with operable esophageal cancer is frequently missed by current noninvasive tumor staging. Here we applied an immunocytochemical cytokeratin assay that allows identification of individual esophageal carcinoma cells disseminated to bone marrow. Prior to therapy, bone marrow was aspirated from the upper iliac crest of 71 patients with esophageal cancer at various disease stages as well as an age-matched control group of 20 noncarcinoma patients. Tumor cells in cytologic bone marrow preparations were detected with monoclonal antibodies (mAbs) CK2, KL1, and A45-B/B3 to epithelial cytokeratins (CKs) using the alkaline phosphatase antialkaline phosphatase method. CK-positive cells were found in 14 (36.8%) of 38 cancer patients treated with curative intent and 16 (48.5%) of 33 patients with extended disease. The overall frequency of these cells was 1 per 4 x 10(5) to 82 per 4 x 10(5) mononuclear cells with no significant differences between patients at different tumor stages. After a short median follow-up of 9.5 months (3-24 months), 7 of 11 patients who underwent complete surgical resection but had tumor cells in bone marrow presented with tumor relapse compared to 2 of 19 corresponding patients without such cells ($p < 0.01$). It was concluded that although bone marrow is not a preferential site of overt metastasis of esophageal cancer, the frequent occurrence of isolated tumor cells at this distant site indicates that hematogenous dissemination of viable malignant cells occurs early in tumor progression.

L9 ANSWER 16 OF 30 MEDLINE
AN 96303978 MEDLINE
DN 96303978
TI [Immunocytochemical detection and prognostic significance of **epithelial tumor** cells in bone marrow of patients with pancreatic carcinoma].
Immunzytochemischer Nachweis und prognostische Bedeutung von epithelialen Tumorzellen im Knochenmark bei Patienten mit Pankreaskarzinomen.
AU Thorban S; Roder J D; **Pantel K**; Siewert J R
CS Chirurgische Klinik und Poliklinik, Technischen Universitat Munchen.
SO ZENTRALBLATT FUR CHIRURGIE, (1996) 121 (6) 487-9; discussion 490-2.
Journal code: Y5I. ISSN: 0044-409X.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 199612
AB INTRODUCTION: Minimal residual disease in patients with operable pancreas carcinoma is frequently missed by current non-invasive tumor staging. PURPOSE: We applied an immunocytochemical cytokeratin assay that allows the identification of individual pancreas carcinoma cells disseminated to bone marrow. METHODS: Prior to therapy bone marrow was aspirated from the upper iliac crest of 42 patients with pancreas carcinoma and a control group of 30 non-carcinoma patients. Tumor cells in cytologic bone marrow preparations were detected with monoclonal antibodies (mAbs) CK2, KL1 and A45-B/B3 to epithelial cytokeratins (CK), using the APAAP-method.
RESULTS:
CK-positive cells were found in 14 (58.3%) of 24 cancer patients treated in curative intent and 10 (55.6%) of 18 patients with extended disease. After a mean follow up of 12.7 (3-32) months, 6 (42.8%) out of 14 patients

who underwent complete surgical resection presented with tumor relapse and 5 (35.7%) with distant metastases as compared to none of 10 corresponding patients without such cells ($p < 0.04$). Moreover, patients with **epithelial tumor** cells in bone marrow showed also a significantly shorter overall survival than those without tumor cells ($p < 0.03$). CONCLUSION: Immunocytochemical screening for **epithelial tumor** cells in bone marrow might contribute to an improved staging and is of prognostic relevance for pancreas carcinoma patients.

L9 ANSWER 17 OF 30 MEDLINE DUPLICATE 9
AN 96255880 MEDLINE
DN 96255880
TI **Epithelial tumour** cells in bone marrow of patients with pancreatic carcinoma detected by immunocytochemical staining.
AU Thorban S; Roder J D; **Pantel K**; Siewert J R
CS Department of Surgery, Technische Universitat Munchen, Germany.
SO EUROPEAN JOURNAL OF CANCER, (1996 Feb) 32A (2) 363-5.
Journal code: ARV. ISSN: 0959-8049.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199610
AB In the present study, epithelial cells in the bone marrow of 42 patients with pancreatic carcinoma were identified immunocytochemically with monoclonal antibodies (MAbs) CK2, KL1 and A45-B/B3 directed to epithelial cytokeratins (CK), using the alkaline phosphatase anti-alkaline phosphatase method. The specificity of the MAbs was demonstrated by negative staining of marrow from 25 non-carcinoma age-matched control patients. Analysis of bone marrow aspirates from cancer patients revealed CK-positive cells in 14 (58.3%) of 24 cancer patients treated with curative intent and 10 (55.6%) of 18 patients with extended disease. After a median follow-up of 15.6 months (range 3-31 months), 5 (35.7%) out of 14 patients who underwent complete surgical resection but had tumour cells in bone marrow presented with distant metastasis and 6 (42.9%) with local relapse as compared to none of 10 corresponding patients without such cells ($P < 0.05$). The described technique may help to identify patients with pancreatic cancer and potential high risk of early metastatic relapse. The results promise to be of important assistance in determining prognosis and consequences in therapy of early stage pancreatic cancer.

L9 ANSWER 18 OF 30 MEDLINE
AN 97031805 MEDLINE
DN 97031805
TI Detection of minimal disease in patients with solid tumors.
AU **Pantel K**
CS Institut fur Immunologie, Ludwig-Maximilians-Universitat Munchen, Germany.
SO JOURNAL OF HEMATOTHERAPY, (1996 Aug) 5 (4) 359-67. Ref: 98
Journal code: B3T. ISSN: 1061-6128.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199704
EW 19970404
AB The detection and elimination of minimal systemic disease in patients with solid tumors is one of the main current topics in clinical oncology. The present review focuses, therefore, on new diagnostic approaches to identify minimal disease in peripheral blood, bone marrow, and lymph nodes of patients with epithelial cancer as the major type of solid tumors in Western industrialized countries. These approaches may be used to improve tumor staging and monitoring of adjuvant therapies, as well as to detect tumor cell contamination in autologous stem cell grafts. Most investigators have developed either immunocytochemical assays with monoclonal antibodies to a variety of epithelial-specific cytoskeleton and membrane antigens or molecular methods based on the extensive amplification of a specific (c)DNA sequence by the polymerase-chain reaction (PCR). In immunocytochemical assays, antibodies to cytokeratins can be regarded as the most specific and sensitive probes to detect isolated **epithelial tumor** cells in bone marrow and blood. Molecular methods are based on the detection of either mutations in oncogenes and tumor suppressor genes (e.g., ki-ras and p53 genes) or the mRNA expression of tissue-specific and tumor-associated genes. mRNA species targeted in these assays encode cytokeratins, prostate-specific antigen, prostate-specific membrane antigen, carcinoembryonic antigen, and polymorphic-epithelial mucin. To introduce the available methods into clinical practice, standardized protocols need to be developed and validated in multi-center studies.

L9 ANSWER 19 OF 30 MEDLINE
AN 97015408 MEDLINE
DN 97015408
TI Immunocytochemical detection of isolated **epithelial tumor** cells in bone marrow of patients with pancreatic carcinoma.
AU Thorban S; Roder J D; **Pantel K**; Siewert J R
CS Department of Surgery, Technische University Munich, Germany.
SO AMERICAN JOURNAL OF SURGERY, (1996 Sep) 172 (3) 297-8.
Journal code: 3Z4. ISSN: 0002-9610.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199701
EW 19970104
AB Epithelial cells in the bone marrow of 42 patients with pancreatic carcinoma were identified immunocytochemically with monoclonal antibodies directed to epithelial cytokeratins. The occurrence of tumor relapse in patients who underwent complete surgical resection was significantly associated with cytokeratin-positivity in bone marrow. The presence of these cells in indicative of an increased disseminative capability of the primary tumor and defines a new category of patients for neoadjuvant

therapy.

L9 ANSWER 20 OF 30 MEDLINE
AN 96217416 MEDLINE
DN 96217416
TI Detection of genetic alterations in micrometastatic cells in bone marrow of cancer patients by fluorescence in situ hybridization.
AU Muller P; Weckermann D; **Riethmuller G**; Schlimok G
CS II. Medizinische Klinik, Zentralklinikum Augsburg, Germany.
SO CANCER GENETICS AND CYTOGENETICS, (1996 May) 88 (1) 8-16.
Journal code: CMT. ISSN: 0165-4608.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199609
AB Detection of micrometastatic tumor cells in bone marrow of cancer patients has been shown to be of prognostic significance. To further characterize these cells, we combined antibody labeling and fluorescence in situ hybridization (FISH). For detection of numerical changes of chromosome 17, nine patients with proven breast cancer whose bone marrow contained **epithelial tumor** cells were evaluated. **Epithelial** cells were stained by anticytokeratin antibody. Afterwards FISH was performed using an alpha-satellite probe specific for chromosome 17. In a second series bone marrow epithelial cells of eight patients with breast cancer and of six with prostatic cancer were evaluated for the amplification of HER-2/neu by using a gene-specific DNA probe. In the first series four patients had only single epithelial cells in their bone marrow. Only one single cell showed five hybridization signals, whereas all other single cells showed two or less. Five patients had clusters of epithelial cells in bone marrow with or without additional single cells. One hundred four cells had three or more hybridization signals and 103 of these polysomic cells were located in tumor cell clusters. In the second series we could detect HER-2/neu amplification in bone marrow **epithelial tumor** cells in two of eight patients with breast cancer but in none of the prostatic cancer patients. These results show that it is possible to detect numerical chromosomal changes and oncogene amplification in bone marrow micrometastatic epithelial cells of cancer patients by combining immunophenotyping and FISH.

L9 ANSWER 21 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:126136 BIOSIS
DN PREV199698698271
TI Methods for detection of micrometastatic carcinoma cells in bone marrow, blood and lymph nodes.
AU **Pantel, K. (1)**; Riethmueller, G.
CS (1) Inst. Immunol., Ludwig Maximilians Univ. Muenchen, Goethestrasse 31, D-80336 Muenchen Germany
SO Onkologie, (1995) Vol. 18, No. 5, pp. 394-401.
ISSN: 0378-584X.
DT General Review
LA English
SL English; German

AB The present review focuses on diagnostic approaches to identify patients with minimal residual epithelial cancer. Epithelial malignancies are the most common forms of cancer in Western industrialized countries. The failure to decrease the mortality of patients with epithelial tumors is most likely due to early dissemination of cancer cells to secondary sites, which is usually missed by conventional diagnostic procedures used for tumor staging. Therefore, over the past ten years sensitive assays have been developed to detect individual carcinoma cells disseminated to regional lymph nodes or distant organs. Among the distant organs, bone marrow has appeared as the most important indicator site where hematogeneously spread cancer cells, can be detected. With regard to detection techniques, most investigators have used either immunocytochemical assays or molecular methods based on the polymerase chain reaction (PCR). Monoclonal antibodies to a variety of 'epithelial-specific' cytoskeleton and membrane antigens have been applied in immunocytochemical assays. At present, antibodies to cytokeratins can be regarded as the most specific and sensitive probes to detect isolated **epithelial tumor** cells in bone marrow. However, in lymph nodes the detection of disseminated epithelial cells is hampered because of the expression of cytokeratins by lymphatic reticulum cells. Presently PCR-based methods are applied to detect tumor-associated mutations of the ki-ras and p53 genes, or mRNA from 'tissue-specific' genes. Thus far, almost all data on the prognostic significance of microdisseminated cells are based on immunocytochemical analyses, whereas the molecular genetic assays still need to be validated in clinical trials. In order to introduce the available methods into international tumor classifications, standardized protocols need to be developed and validated in multicenter studies.

L9 ANSWER 22 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:55745 BIOSIS
DN PREV199598070045
TI Immunocytochemical screening for occult **epithelial tumor** cells in bone marrow.
AU **Pantel, K. (1)**; Schlimok, G. (1); Angstwurm, M.; Schmaus, W.; Riethmueller, G.
CS (1) Inst. Immunologie, Ludwig-Maximilians-Univ., Muenchen Germany
SO Blood, (1994) Vol. 84, No. 10 SUPPL. 1, pp. 353A.
Meeting Info.: Abstracts Submitted to the 36th Annual Meeting of the American Society of Hematology Nashville, Tennessee, USA December 2-6, 1994
ISSN: 0006-4971.
DT Conference
LA English

L9 ANSWER 23 OF 30 MEDLINE
AN 95128653 MEDLINE
DN 95128653
TI Methodological analysis of immunocytochemical screening for disseminated **epithelial tumor** cells in bone marrow.
AU **Pantel K**; Schlimok G; Angstwurm M; Weckermann D; Schmaus W; Gath H; Passlick B; Izbicki J R; **Riethmuller G**
CS Institut fur Immunologie, Ludwig-Maximilians-Universitat, Munchen, Germany.
SO JOURNAL OF HEMATOTHERAPY, (1994 Fall) 3 (3) 165-73.

Journal code: B3T. ISSN: 1061-6128.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199504
AB The emerging clinical relevance of bone marrow micrometastasis has prompted several investigations, using a variety of immunocytochemical approaches. The present study was designed to evaluate some of the variables affecting the immunocytochemical detection of individual **epithelial tumor** cells in bone marrow. Using an alkaline phosphatase-antialkaline phosphatase staining technique, we evaluated bone marrow aspirates from 358 patients with primary carcinomas of the breast (n = 150), lung (n = 66), prostate (n = 42), or colorectum (n = 100). Individual tumor cells in cytological preparations were detected with monoclonal antibody (MAb) CK2 to the epithelial cytokeratin component 18 (CK18), which has been validated in extensive clinical studies. In addition, the utility of the broad-spectrum MAb A45-B/B3 was explored in this study. The high specificity of MAbs CK2 and A45-B/B3 was supported by analysis of bone marrow from 75 noncarcinoma control patients and by double-marker analysis with MAbs to mesenchymal marker proteins (CD45 and vimentin). In contrast, MAbs E29 and HMFG1, directed to mucin-like epithelial membrane proteins, cross-reacted with hematopoietic cells in 26.7-42.7% of all samples tested. The majority of the 154 positive samples (43.0%) from cancer patients displayed less than 10 CK18-positive cells per 8 x 10(5) marrow cells analyzed. The detection rate, however, was affected by blood contamination of the aspirate, the number of aspirates analyzed, and the number of marrow cells screened per aspiration site. Comparative immunostaining of bone marrow specimens with MAbs CK2 and A45-B/B3 indicated that downregulation of CK18 in micrometastatic carcinoma cells occurs in about 50% of the 172 samples analyzed, regardless of the primary tumor origin.(ABSTRACT TRUNCATED AT 250 WORDS)

L9 ANSWER 24 OF 30 MEDLINE DUPLICATE 10
AN 94353532 MEDLINE
DN 94353532
TI Immunocytochemical detection and phenotypic characterization of micrometastatic tumour cells in bone marrow of patients with prostate cancer.
AU Oberneder R; Riesenberg R; Kriegmair M; Bitzer U; Klammert R; Schneede P; Hofstetter A; **Riethmuller G**; **Pantel K**
CS Urologische Universitatsklinik, Klinikum Grosshadern, Munchen, Germany..
SO UROLOGICAL RESEARCH, (1994) 22 (1) 3-8.
Journal code: WRX. ISSN: 0300-5623.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199412
AB Monoclonal antibodies (mAbs) specific for cytokeratins are potent probes for the identification of disseminated individual **epithelial tumour** cells in mesenchymal organs such as bone marrow. We have used a monoclonal antibody (mAB) against cytokeratin 18 (CK18) for the

detection of individual metastatic tumour cells in bone marrow aspirates from 84 patients with carcinoma of the prostate. CK18+ cells were detected in a sensitivity of 1 per 8 x 10(5) marrow cells using the alkaline phosphatase anti-alkaline phosphatase (APAAP) system for staining. We were able to detect CK18+ tumour cells in the marrow of 33% of patients with stage N0M0 prostate cancers. The incidence of CK18+ cells showed a significant correlation with established risk factors, such as local tumour extent, distant metastases and tumour differentiation. For further characterization of such cells in patients with prostate cancer, we developed an immunocytochemical procedure for simultaneous labelling of cytokeratin component no. 18 (CK18) and prostate-specific antigen (PSA). In a first step, cells were incubated with a murine mAb against PSA, followed by gold-conjugated goat anti-mouse antibodies. In a second step, a biotinylated mAb to CK18 was applied as primary antibody and subsequently incubated with complexes of streptavidin-conjugated alkaline phosphatase, which were developed with Newfuchsin substrate. The binding of gold-labelled antibodies was visualized by silver enhancement. CK18+ cells co-expressing PSA were found in bone marrow aspirates from 5 out of 14 patients with carcinomas of the prostate. The specificity of CK18 for **epithelial tumour** cells in bone marrow was supported by negative staining of 12 control aspirates from patients with benign prostatic hyperplasia (BPH).(ABSTRACT TRUNCATED AT 250 WORDS)

L9 ANSWER 25 OF 30 MEDLINE DUPLICATE 11
AN 93353545 MEDLINE
DN 93353545
TI Differential expression of proliferation-associated molecules in individual micrometastatic carcinoma cells.
AU **Pantel K**; Schlimok G; Braun S; Kutter D; Lindemann F; Schaller G; Funke I; Izbicki J R; **Riethmuller G**
CS Institut fur Immunologie, Munich, Federal Republic of Germany.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1993 Sep 1) 85 (17) 1419-24. Journal code: J9J. ISSN: 0027-8874.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199311
AB BACKGROUND: The development of monoclonal antibodies (MAbs) to cytokeratins, which are integral components of the epithelial cytoskeleton, has made possible immunocytochemical detection of **epithelial tumor** cells. Importantly, this technique allows the detection of **epithelial tumor** cells that have metastasized from primary adenocarcinomas to secondary sites such as the bone marrow. PURPOSE: The aim of the study was not only to detect micrometastatic cells in bone marrow, but also to assess the expression of nuclear proliferation markers (Ki-67 and p120) and the erbB2 oncogene (also known as ERBB2) in these cells and, thus, hopefully improve prognostic precision. METHODS: Bone marrow aspirates were obtained from both sides of the upper iliac crest of 532 patients having definitive diagnoses of either breast or gastrointestinal cancer. The presence of micrometastatic **epithelial tumor** cells in bone marrow was assayed using the MAb cytokeratin 2 (CK2) to cytokeratin component 18 (CK18), in combination with the alkaline phosphatase-anti-alkaline

phosphatase immunostaining technique. After primary screening of all marrow samples with MAb CK2, representative subgroups of CK18+ samples were selected for co-labeling with MAbs either to ErbB (n = 16), ErbB2 (n = 121), Ki-67 (n = 33), or p120 (n = 36) protein. An alternative labeling protocol based on the combination of immunogold and immunoenzymatic techniques was utilized to confirm the results derived from immunoenzymatic double staining. RESULTS: In total, single CK18-positive tumor cells were detected in 180 (33.8%) of 532 bone marrow aspirates, with few differences among patients with breast or gastrointestinal cancer in TNM stage M0 (i.e., no distant metastasis). In patients with overt metastasis (stage M1), however, the incidence of metastatic cells in marrow increased to 73.7% in breast cancer, 52.5% in gastric cancer, and 39.0% in colon cancer. Whereas expression of Ki-67 or p120 on micrometastatic cells was observed only in 11 (15.9%) of 69 cancer patients analyzed, ErbB2+/CK18+ cells were found in 48 (67.6%) of 71 breast cancer patients and 14 (28.0%) of 50 patients with gastrointestinal cancer (P = .0001). The incidence of ErbB2+/CK18+ cells was positively correlated with the clinical stage of tumor progression. CONCLUSIONS: The high incidence of ErbB2 expression on micrometastatic breast cancer cells in the bone marrow suggests that these cells might have been positively selected during early stages of metastasis. The majority of these cells appear to be in a dormant state of cell growth. IMPLICATIONS: Although support from clinical follow-up is still needed, this study demonstrates that, beyond the mere presence of micrometastatic cells in bone marrow, useful prognostic information can be obtained by analysis of additional cell growth markers.

L9 ANSWER 26 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1993:359109 BIOSIS
DN PREV199345042534
TI Assessment of the growth potential of individual **epithelial tumor** cells present in bone marrow of cancer patients.
AU **Pantel, K.**; Schlimok, G.; Hoechtlen-Vollmar, W.; Kutter, D.; Schnaus, W.; Braun, S.; Riethmueller, G.
CS Inst. Immunol., Munich Germany
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1993) Vol. 34, No. 0, pp. 62.
Meeting Info.: 84th Annual Meeting of the American Association for Cancer Research Orlando, Florida, USA May 19-22, 1993
ISSN: 0197-016X.
DT Conference
LA English

L9 ANSWER 27 OF 30 MEDLINE DUPLICATE 12
AN 93224339 MEDLINE
DN 93224339
TI Immunocytochemical double staining of cytokeratin and prostate specific antigen in individual prostatic tumour cells.
AU Riesenberg R; Oberneder R; Kriegmair M; Epp M; Bitzer U; Hofstetter A; Braun S; **Riethmuller G**; **Pantel K**
CS Urologische Klinik im Klinikum Grosshadern, Munchen, Germany..
SO HISTOCHEMISTRY, (1993 Jan) 99 (1) 61-6.
Journal code: G9K. ISSN: 0301-5564.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 199307
AB Early dissemination of malignant cells is the main cause for metastatic relapse in patients with solid tumours. By use of monoclonal antibodies (mAbs) specific for cytokeratins, disseminated individual **epithelial tumour** cells can now be identified in mesenchymal organs such as bone marrow. Further to characterize such cells in patients with prostate cancer, an immunocytochemical procedure was developed for simultaneous labelling of cytokeratin component no. 18 (CK18) and prostate specific antigen (PSA). In a first step, cells were incubated with mAb ER-PR8 against PSA and secondary gold-conjugated goat anti-mouse antibodies. In a second step, biotinylated mAb CK2 to CK18 was applied as primary antibody and subsequently incubated with complexes of streptavidin-conjugated alkaline phosphatase, which were developed with the Newfuchsin substrate. The binding of gold-labelled antibodies was visualized by silver enhancement. The sensitivity and specificity of the technique was demonstrated on cryostat sections of hyperplastic prostatic tissue, and cytological preparations of LNCaP prostatic tumour cells. Double staining was restricted to cells derived from the secretory epithelium of the prostate. Cross-reactivity between both detection systems was excluded by several controls, including the use of unrelated antibodies of the same isotype and the staining of CK18+/PSA- HT29 colon carcinoma cells. CK18+ cells co-expressing PSA were found in bone marrow aspirates from 5 out of 13 patients with carcinomas of the prostate, a finding that is consistent with the relative fraction of double-positive LNCaP cells. The specificity of CK18 for **epithelial tumour** cells in bone marrow was supported by negative staining of 12 control aspirates from patients with benign prostatic hypertrophy.(ABSTRACT TRUNCATED AT 250 WORDS)

L9 ANSWER 28 OF 30 MEDLINE
AN 90237837 MEDLINE
DN 90237837
TI **Epithelial tumor** cells in bone marrow of patients with colorectal cancer: immunocytochemical detection, phenotypic characterization, and prognostic significance.
AU Schlimok G; Funke I; Bock B; Schweiberer B; Witte J; **Riethmuller G**
CS Medical Clinic II, Zentralklinikum, Augsburg, Federal Republic of Germany.
SO JOURNAL OF CLINICAL ONCOLOGY, (1990 May) 8 (5) 831-7.
Journal code: JCO. ISSN: 0732-183X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199008
AB A monoclonal antibody (mAb) directed against the cytokeratin (CK) polypeptide no. 18 specifically expressed in cells derived from simple epithelia was used to detect **epithelial tumor** cells in bone marrow aspirates. Of 156 patients with colorectal carcinoma, 42 presented with cells at the time of primary surgery. The incidence of positive findings varied considerably with the size and the localization of the primary tumor, the involvement of regional lymph nodes, and the presence of clinically manifest metastases. Applying a sensitive double-staining procedure, we could demonstrate that epithelial cells in

bone marrow showed a heterogeneic expression of receptors for epidermal growth factor (EGF-R) and transferrin (Tf-R) as well as of the proliferation-associated Ki67 antigen. Also human leukocyte antigen (HLA) class I antigens differed widely in their expression on the CK-positive cells. Clinical follow-up studies on 85 patients showed a significantly higher relapse rate in patients presenting with CK-positive cells in their bone marrow at the time of primary surgery. Twenty-three patients were monitored for the presence or absence of CK-positive cells in bone marrow over time. The majority of monitored patients (18 of 23) exhibited a constant pattern of immunocytochemical findings during the time of observation. Thus, the technique may be useful in identifying high-risk patients as well as in monitoring adjuvant therapeutic trials.

L9 ANSWER 29 OF 30 MEDLINE
AN 88280925 MEDLINE
DN 88280925
TI [Monoclonal antibodies--new probes for diagnosis and therapy. Their use as an example of the micrometastasizing of solid tumors].
Monoklonale Antikorper--neue Sonden fur Diagnose und Therapie. Ihr Einsatz am Beispiel der Mikrometastasierung solider Tumoren.
AU Schlimok G; Funke I; Bock B; Schweiberer B; **Riethmuller G**
CS Institut fur Immunologie, Universitat Munchen..
SO ARZNEIMITTEL-FORSCHUNG, (1988 Mar) 38 (3A) 435-7. Ref: 7
Journal code: 91U. ISSN: 0004-4172.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA German
FS Priority Journals
EM 198810
AB Monoclonal antibody CK2, recognizing component No. 18, appeared to be the most suitable reagent for the detection of **epithelial tumor** cells in bone marrow. Its specificity was confirmed in a double-marker staining procedure (combination of APAAP-technique and radioautography). CK2 positive cells were demonstrated not to reveal any cross-reactivity with an antibody directed against the "leucocyte common antigen". A significant correlation between the presence of **epithelial tumor** cells in bone marrow and certain conventional risk factors was found. A more detailed phenotypic characterisation could demonstrate the expression of proliferation associated antigens on these cells. Furthermore in an immunotherapeutic approach with monoclonal antibody 17-1A, labelling of the disseminated tumor cells in bone marrow after infusion of the antibody was shown.

L9 ANSWER 30 OF 30 MEDLINE
AN 86302595 MEDLINE
DN 86302595
TI In vivo and in vitro labelling of **epithelial tumor** cells with anti 17-1A monoclonal antibodies in bone marrow of cancer patients.
AU Schlimok G; Gottlinger H; Funke I; Swierkot S; Hauser H; **Riethmuller G**
SO HYBRIDOMA, (1986 Jul) 5 Suppl 1 S163-70.

Journal code: GFS. ISSN: 0272-457X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198612